
In the name of
ALLAH
SAMATAK.COM

Iranian Endocrine Society Guidelines for Screening, Diagnosis, and Management of Gestational Diabetes Mellitus

Int J Endocrinol Metab. 2021January

Majid Valizadeh , Farhad Hosseinpanah , Fahimeh Ramezani Tehrani , Hengameh Abdi , Ladan Mehran , Farzad Hadaegh , Atieh Amouzegar , Farzaneh Sarvghadi , Fereidoun Azizi and
Iranian Endocrine Society Task Force

(+ ADA 2022)

Context

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance, with the onset or first detection during pregnancy

Previous studies have reported the association of GDM with the risk of adverse pregnancy outcomes, such as

I. preeclampsia,
II.macrosomia,
III.shoulder dystocia,

which may lead to operative vaginal delivery and birth trauma.

Gestational diabetes mellitus is also associated with unfavorable long-term outcomes,such as :

I.the development of type 2 diabetes in mothers

II. obesity,diabetes mellitus (DM), and cardiovascular diseases in offspring

On the other hand, the early diagnosis and management of GDM *can prevent*

I. macrosomia,

II. shoulder dystocia,

III. preeclampsia,

IV. hypertensive disorders during pregnancy

Therefore, screening for diagnosis and management of GDM is of paramount importance.

The *prevalence* of GDM varies greatly from 0.6-3.6% in North Europe to 6.3% in Italy due to various diagnostic criteria in different populations.

Along with an increase in the prevalence of risk factors for diabetes, such as obesity, high maternal age,and family history of DM,GDM has also shown an increasing trend(e.g.,6-7% in the United States and 7.1% in India)

According to a recent systematic review,the overall prevalence of GDM,based on the diagnostic criteria of the International Association of Diabetes in Pregnancy Study Group (IADPSG), is 10.6% versus a pooled overall prevalence of 4.4%,regardless of the type of screening thresholds

Moreover,a systematic review of all studies conducted up to 2012 in *Iran* reported the overall prevalence of GDM to be 3.4% based on old diagnostic criteria,ranging widely from 1.3% to 18.5%

On the other hand, the increasing prevalence of overweight and obesity in recent years has been associated with the increasing prevalence of GDM, based on the IADPSG criteria, which exceeds all previous records.

In this regard,two recent Iranian studies from Isfahan and Tehran reported the higher prevalence of GDM based on the IADPSG criteria (15.6% and 9.3%, respectively) than based on the old two-step criteria(7.1% and 4.2%, respectively).

Moreover, two recent meta-analyses, one including nine observational studies and one including four clinical trials, showed adverse pregnancy and prenatal outcomes in GDM patients diagnosed by either method.

However, the associations were stronger in the two-step approach than in the one-step approach

Considering the mentioned conflicting results, the World Health Organization (WHO) suggested that the final decision about screening, diagnosis, and management of GDM be made for each country, depending on the prevalence rates, risk factors, percapita health expenditure, local obstacles, resources, and priorities of that particular country.

To follow this recommendation, Ramezani et al.have conducted a randomized community non-inferiority trial among more than 30,000 pregnant women in five different regions of Iran

The participants were randomly assigned to one of the five GDM screening methods (in-cluding one-step and two-step methods), based on various cutoff points for fasting plasma glucose (FPG) and abnormal results for GDM diagnosis.

The pregnancy outcomes,quality of life, and cost of healthcare are recorded in detail.

The results of this study can provide valuable evidence on the diagnosis and management of GDM, as prevention of adverse outcomes of GDM can be cost-effective

Evidence Acquisition

The Iranian Endocrine Society constituted a task force, consisting of obstetrician-gynecologists, endocrinologists, a clinical nutritionist, a clinical epidemiologist, and a librarian, to review the published literature and prepare a national guideline for the diagnosis and management of GDM

International and national clinical practice guidelines and consensuses, systematic reviews, and their references were reviewed.

Several group meetings were held, and a consensus was reached on all recommendations with a majority decision.

To formulate evidence-based recommendations, the Iranian Endocrine Society task force followed the approach recommended By the American College of Physicians' Guideline Grading System

Table 1.

The American College of Physicians' Guideline Grading System (14)

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden OR Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced with Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks.		

Results

Screening and Management of Diabetes Before and During Pregnancy

Evaluation of Dysglycemia Before Pregnancy

Question 1

Who should be assessed for dysglycemia among women contemplating pregnancy?

Recommendation 1

Among women who present for preconception counseling, all non-diabetic women with at least one of the known risk factors must be screened for dysglycemia

(Strong recommendation, low-quality evidence)

Box 1.

Risk Factors for Gestational Diabetes Mellitus (GDM) (8, 10, 15-17)

Risk Factors
1. Previous history of GDM
2. History of diabetes mellitus in first-degree relatives
3. Known glucose intolerance
4. Obesity (BMI ≥ 30 kg/m^2)
5. Low physical activity[a] (18, 19)
6. History of polycystic ovarian syndrome (PCOS)
7. History of hypertension and/or taking antihypertensive medication
8. Serum TG > 250 mg/dL and/or HDL< 35 mg/dL
9. History of stillbirth[b]
10. History of congenital anomalies or macrosomia[c] in the offspring

Abbreviations: BMI, body mass index; TG, triglycerides; HDL, high-density lipoprotein.

[a]Physical activity level is defined as low (MET < 600 min/week), moderate (MET 600 - 1499 min/week), and high (MET ≥ 1500 min/week), based on the Persian-translated Modifiable Activity Questionnaire (MAQ).

[b]Stillbirth refers to intrauterine fetal death after 20 weeks of gestation.

[c]Birth of an infant ≥ 4000 g.

Question 2

How should women at risk for dysglycemia be screened before pregnancy, and what are the diagnostic criteria?

Recommendation 2

The screening tests and diagnostic criteria for women before pregnancy are similar to those for non-pregnant women

(Strong recommendation, low-quality evidence).

Considering the ease, feasibility, and availability, we suggest the measurement of fasting plasma glucose (FPG).

Table 2.

Diagnostic Criteria for Glucose Intolerance Before Pregnancy [a, b]

	Normal	Prediabetes	Diabetes
Fasting plasma glucose (mg/dL)	< 100	100 - 125	≥ 126
Two-hour plasma glucose during OGTT (mg/dL)	< 140	140 - 199	≥ 200
HbA1C (%)	< 5.7	5.7 - 6.4	≥ 6.5

[a]Having a random plasma glucose ≥ 200 mg/dL with classic symptoms of hyperglycemia is also defined as diabetes.

[b]In the absence of overt hyperglycemia, the diagnosis should be based on two abnormal tests, the same or different tests.

Question 3

How should women with glucose intolerance be followed up?

Recommendation 3

Women with impaired fasting glucose (IFG) are recommended to adhere to an appropriate diet and moderate-intensity exercise (30 min per day or 150 min per week).

In overweight and obese women, the goal of non-pharmacological measures is to achieve at least 7% weight loss

(Strong recommendation, low-quality evidence).

There is no strong evidence that pre-gestational IFG can lead to fetal loss or abnormalities;

however, women with IFG should be more careful due to the higher risk of GDM

There is also insufficient evidence regarding the effect of preventive metformin therapy on the risk of pregnancy complications or GDM

Recommendation 4

Metformin is *not recommended* for the prevention of GDM in women with polycystic ovary syndrome (PCOS) and infertility, who become pregnant while taking metformin

(Strong recommendation, moderate-quality evidence).

Overall, in women with PCOS and infertility, who become pregnant while taking metformin, there is no strong evidence regarding the preventive effect of metformin on the risk of GDM;

however, metformin seems to reduce the risk of fetal loss during the first trimester

Diagnosis of Diabetes During Pregnancy

Diabetes Screening in the First Prenatal Visit

Question 4

Who should be evaluated for diabetes in the first prenatal visit and what are the recommended tests?

Recommendation 5

Fasting plasma glucose must be measured (at least eight hours after the last meal) in all women with normal glucose homeostasis in the past year and no history of diabetes, presenting for their first prenatal visit

(Strong recommendation, low-quality evidence).

Due to the outbreak of obesity, diabetes has become more prevalent at a young age during fertility years.

Therefore, there are concerns about undetected diabetes during pregnancy and its adverse effects on the mother and the fetus.

There has been an increasing trend of overweight, obesity, and abdominal obesity in Iran, which are more common among women than men

Many scientific communities, including the American Diabetes Association, have recommended screening in the first prenatal visits only for women with diabetes risk factors, based on the pre-gestational criteria

The American College of Obstetricians and Gynecologists (ACOG) has also made similar recommendations for diabetes screening in early pregnancy.

Generally, the best screening method in early pregnancy has not been defined yet.

However, due to the low cost of test and also the increasing prevalence of overweight and obesity in Iran, we recommend FPG measurement in the first prenatal visit.

Question 5

What are the diagnostic criteria for diabetes in early pregnancy and how are the results interpreted?

Recommendation 6

In the first prenatal visit, pregnant women with FPG ≥ 126 mg/dL in at least two separate sample tests (*without delay*) are diagnosed with overt diabetes, and no further screening tests with glucose load are needed

(Strong recommendation, high-quality evidence)

Recommendation 7

Women with random plasma glucose levels above 200 mg/dL in the presence of classic symptoms of diabetes are diagnosed with overt diabetes

(Strong recommendation, high-quality evidence)

Recommendation 8

In the first prenatal visit, GDM is diagnosed by an FPG level of 100 - 125 mg/dL,

even in one single measurement

(Strong recommendation, low-quality evidence).

Recommendation 9

Women with negative screening in early pregnancy, i.e., FPG < 100 mg/dL, are recommended to be screened at 24 - 28 weeks of gestation

(Strong recommendation, high-quality evidence).

Table 3.

Diagnostic Criteria for Glucose Intolerance Based on Fasting Plasma Glucose Levels (mg/dL) in the First Prenatal Visit

Fasting Plasma Glucose Levels (mg/dL)	Glucose Intolerance
< 100	Normal
100 - 125	Gestational diabetes
≥ 126[a]	Overt or pre-gestational diabetes

[a]Should be confirmed with another separate sample test.

Question 6

Which treatment is used for GDM in early pregnancy?

Recommendation 10

It is recommended for pregnant women with GDM diagnosed in early pregnancy to adhere to an appropriate diet, physical activity, and insulin therapy if needed

(Weak recommendation, low-quality evidence).

Although there is no strong evidence regarding the effect of GDM treatment in early pregnancy, appropriate diet, increased physical activity, self-monitoring of blood glucose (SMBG), and drug therapy (if needed) are recommended for women diagnosed with GDM in early pregnancy.

Question 7

Is hemoglobin A1c (HbA1c) measurement used for the diagnosis of GDM in early pregnancy?

Recommendation 11

At present, the measurement of HbA1c is not recommended for the diagnosis of GDM in Iran

(Strong recommendation, low-quality evidence).

Question 8

Are oral anti-diabetic agents recommended for glycemic control in women with GDM diagnosed in early pregnancy?

Recommendation 12

Prescription of oral anti-diabetic agents is not recommended during the first trimester of pregnancy

(Strong recommendation, low-quality evidence).

Question 9

What are the glycemic goals in the management of GDM diagnosed in early pregnancy?

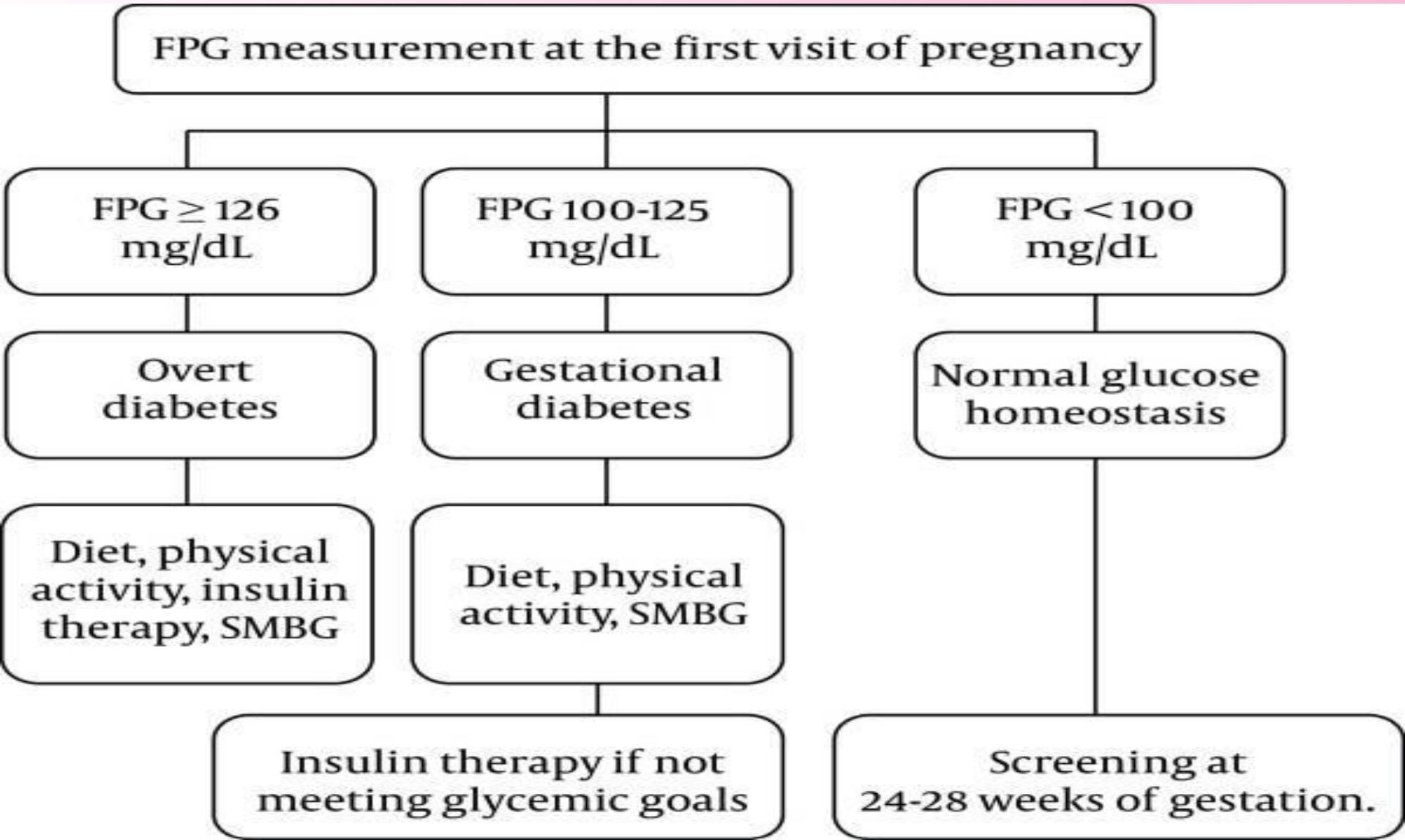
Recommendation 13

The treatment goals during the first trimester of pregnancy are not different from those of other trimesters and include FPG < 95 mg/dL, one-hour postprandial glucose (PPG) < 140 mg/dL, and two-hour PPG < 120 mg/dL

(Weak recommendation, low-quality evidence).

These treatment goals are based on the suggested values for the second half of pregnancy because there is no conclusive evidence regarding the plasma glucose level during the first half of pregnancy.

Algorithm for the screening of diabetes at the first visit of pregnancy.



Screening Diabetes in Pregnant Women with Negative First Screening for GDM

Question 10

Who should be screened for GDM at 24 - 28 weeks of gestation?

Recommendation 14

All pregnant women with negative screening results (FPG < 100 mg/dL) in earlier evaluations should be screened for GDM at 24 - 28 weeks of gestation

(Strong recommendation, moderate-quality evidence).

Question 11

What are the tests used for screening of GDM at 24 – 28 weeks of gestation?

Recommendation 15

For GDM screening at 24 - 28 weeks of gestation, a two-step glucose tolerance test (GTT) is recommended

(Weak recommendation, low-quality evidence)

There is no consensus regarding the best screening method for GDM due to the lack of outcome-based surveys comparing different methods.

Overall, the proposed methods may vary in different populations.

The two-step approach, using 50 g of glucose in the first step, is the most common screening approach in many countries.

Various recommendations and guidelines have been proposed by international scientific communities for the detection of GDM .

However, there have been major controversies over the diagnosis of GDM, using one-step or two-step GTT, based on different glucose thresholds because of inconclusive evidence about these methods for the detection of GDM in pregnant women.

Question 12

What thresholds are considered positive in the 50 g Glucose Challenge Test (GCT)?

Recommendation 16

In GCT with 50 g oral glucose, a plasma glucose level of ≤140 mg/dL is considered to be normal

(Strong recommendation, moderate-quality evidence).

Recommendation 17

Gestational diabetes mellitus is diagnosed if one-hour plasma glucose exceeds 200 mg/dL in 50 g GCT

(Strong recommendation, moderate-quality evidence).

Different thresholds of 130, 135, and 140 mg/dL have been recommended for GCT, with lower thresholds leading to a higher false-positive rate.

Accordingly, ACOG has recommended using higher thresholds .

Table 4.

Diagnostic Criteria of Glucose Challenge Test (GCT) for Pregnant Women without a History of Diabetes at 24 - 28 Weeks of Gestation

One-Hour Plasma Glucose in GCT with 50 g Oral Glucose Solution (mg/dL)	Glucose Intolerance
< 140	Normal
≥ 200	Gestational diabetes
140 - 199	OGTT [a]

[a]100-g oral glucose tolerance test (Table 5).

Question 13

How should pregnant women with positive test results in the first step be evaluated?

Recommendation 18

Patients with one-hour plasma glucose levels of 140 - 199 mg/dL in GCT are recommended to undergo 100 g oral glucose tolerance test (OGTT) after at least eight hours of fasting to measure the plasma glucose levels at one, two, and three hours after receiving glucose

(Strong recommendation, low-quality evidence)

Question 14

What are the criteria for GDM diagnosis using 100 g OGTT?

Recommendation 19

Gestational diabetes mellitus is diagnosed if plasma glucose levels meet or exceed the cutoff points in at least two OGTT samples, I.e., FPG ≥ 95 mg/dL, one-hour PG ≥ 180 mg/dL, two-hour PG ≥ 155 mg/dL, and three-hour PG ≥ 140 mg/dL.

A recent systematic review and meta-analysis of 26 studies reported higher rate of adverse pregnancy outcomes in women with one abnormal result of 100 g OGTT than in those with normal results in all four samples.

accordingly, the last ACOG practice bulletin noted that we *may* diagnose GDM based on *one elevated result* in 100 g OGTT

Recommendation 20

One-step GTT with 75 g oral glucose after overnight fasting, with plasma glucose measurements during fasting and one and two hours post-loading, is unhindered.

Question 15

What are the criteria for GDM diagnosis with 75 g oral glucose?

Recommendation 21

In one-step GTT with 75 g glucose, FPG ≥ 92 mg/dL, one-hour PG ≥ 180 mg/dL, and two-hour PG ≥ 153 mg/dL are considered abnormal, and GDM is diagnosed even if one criterion is met.

Table 5.

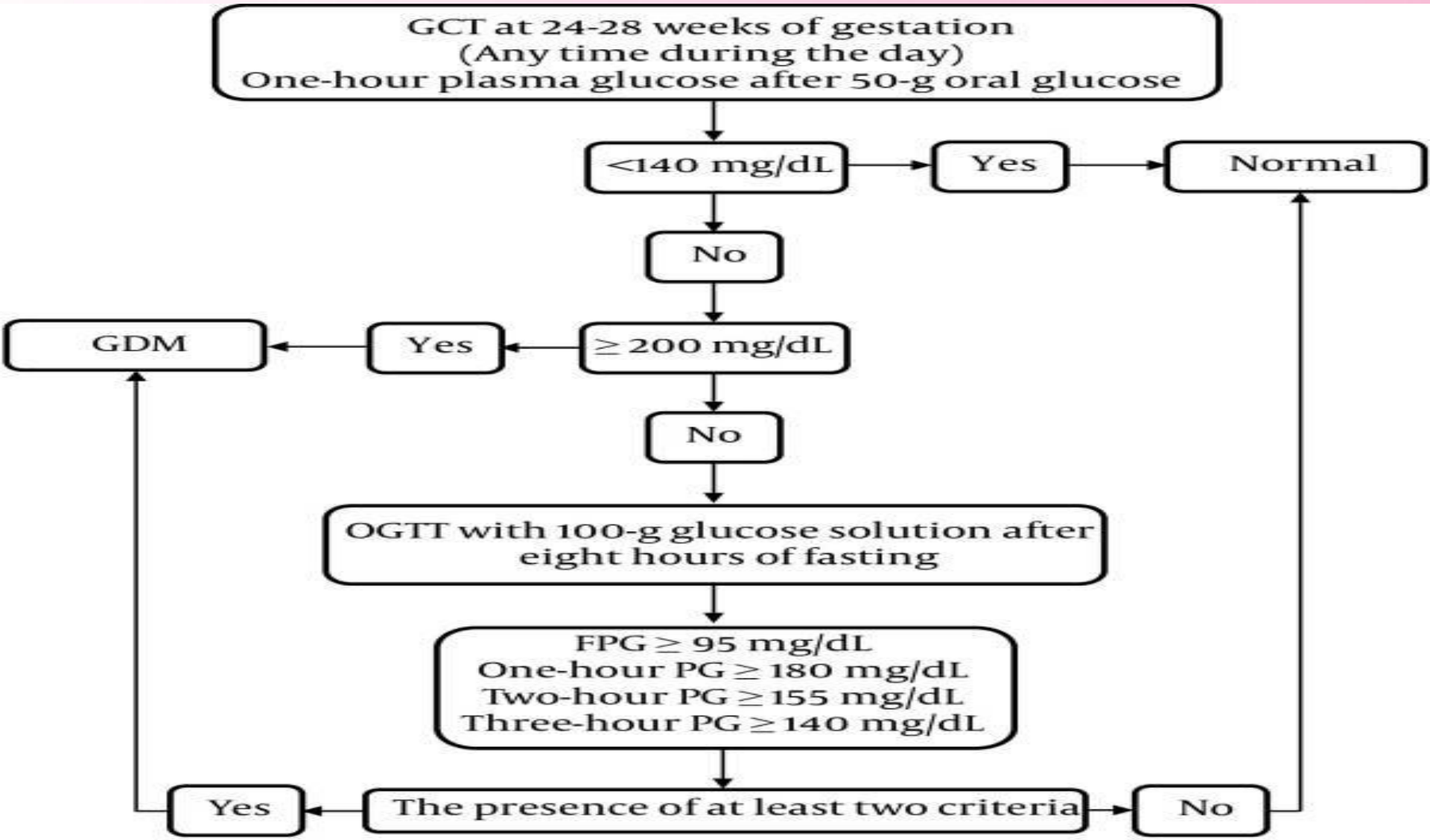
Diagnostic Criteria of GDM in Two-step and One-step Approaches

Measurement Time	100 g OGTT in Two-Step Approach with Carpenter and Coustan Criteria (30)[a]	One-Step Approach with 75 g OGTT[b]
Fasting plasma glucose	95 mg/dL	92 mg/dL
One-hour plasma glucose	180 mg/dL	180 mg/dL
Two-hour plasma glucose	155 mg/dL	153 mg/dL
Three-hour plasma glucose	140 mg/dL	

[a]The diagnosis of GDM is made if at least two of four plasma glucose levels are met or exceeded.

[b]One abnormal value confirms GDM.

The two-step approach for GDM screening at 24 - 28 weeks of gestation



Recommendation 22

Following the diagnosis of GDM, based on any of the above mentioned guidelines, repeating GTT is not necessary

(Strong recommendation, low-quality evidence).

Recommendation 23

If a prenatal complication suggestive of GDM(e.g., macrosomia, polyhydramnios, and fetal waist circumference ≥ 90th percentile) occurs, GTT should berepeated even for women with normal previous evaluations

(Strong recommendation, low-quality evidence)

This recommendation is based on the findings of studies that showed that repeated screening can detect additional cases of GDM, especially in high-risk women .

In such cases, the use of the one-step approach with 75 g oral glucose or a two-step approach (considered positive with only one abnormal glucose result) is less risky.

Management of GDM

Question 16

How GDM should be managed?

Recommendation 24

The management of GDM at 24 - 28 weeks of gestation includes:

- appropriate diet,
- increasing physical activity (at least 150 min/week),
- drug therapy, if needed

(Strong recommendation, high-quality evidence).

Since interventions reducing the serum glucose level improve the outcomes of GDM, especially shoulder dystocia and delivery of a large-for-gestational-age (LGA) infant, the treatment of pregnant women with GDM is effective

ADA 2022

Preconception Counseling

15.1 Starting at puberty and continuing in all women with diabetes and reproductive potential, preconception counseling should be incorporated into routine diabetes care. A

15.2 Family planning should be discussed, and effective contraception (with consideration of long-acting, reversible contraception) should be prescribed and used until a woman's treatment regimen and A1C are optimized for pregnancy. A

15.3 Preconception counseling should address the importance of achieving glucose levels as close to normal as is safely possible, ideally A1C <6.5% (48 mmol/mol), to reduce the risk of congenital anomalies, preeclampsia, macrosomia, and other complications. A

Preconception Care (continued)

15.6 Women with preexisting type 1 or type 2 diabetes who are planning pregnancy or who have become pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy.

Dilated eye examinations should occur ideally before pregnancy or in the first trimester, and then patients should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy and as recommended by the eye care provider. B

Table 15.1—Checklist for preconception care for women with diabetes (17,19)

Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
  - Overweight/obesity or underweight
  - Meal planning
  - Correction of dietary nutritional deficiencies
  - Caffeine intake
  - Safe food preparation technique
- ☐ Lifestyle recommendations for:
  - Regular moderate exercise
  - Avoidance of hyperthermia (hot tubs)
  - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- ☐ Counseling on diabetes in pregnancy per current standards, including: natural history of insulin resistance in pregnancy and postpartum; preconception glycemic targets; avoidance of DKA/severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy; PCOS (if applicable); fertility in patients with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, still birth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy, etc.
- ☐ Supplementation
  - Folic acid supplement (400 μg routine)
  - Appropriate use of over-the-counter medications and supplements

Medical assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including: DKA/severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, NAFLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric/gynecologic history, including history of: cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- ☐ Review of current medications and appropriateness during pregnancy

Screening should include:

- ☐ Diabetes complications and comorbidities, including: comprehensive foot exam; comprehensive ophthalmologic exam; ECG in women starting at age 35 years who have cardiac signs/symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine protein-to-creatinine ratio
- ☐ Anemia
- ☐ Genetic carrier status (based on history):
  - Cystic fibrosis
  - Sickle cell anemia
  - Tay-Sachs disease
  - Thalassemia
  - Others if indicated
- ☐ Infectious disease
  - *Neisseria gonorrhea/Chlamydia trachomatis*
  - Hepatitis C
  - HIV
  - Pap smear
  - Syphilis

Immunizations should include:

- ☐ Rubella
- ☐ Varicella
- ☐ Hepatitis B
- ☐ Influenza
- ☐ Others if indicated

Preconception plan should include:

- ☐ Nutrition and medication plan to achieve glycemic targets prior to conception, including appropriate implementation of monitoring, continuous glucose monitoring, and pump technology
- ☐ Contraceptive plan to prevent pregnancy until glycemic targets are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including: hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction

Gestational Diabetes Mellitus

2.26a In women who are planning pregnancy, screen those with risk factors and consider testing all women for undiagnosed diabetes.

2.26b Before 15 weeks of gestation, test women with risk factors and consider testing all women for undiagnosed diabetes at the first prenatal visit using standard diagnostic criteria, if not screened preconception.

Gestational Diabetes Mellitus (continued)

2.26d Before 15 weeks of gestation, screen for abnormal glucose metabolism to identify women who are at higher risk of adverse pregnancy and neonatal outcomes, are more likely to need insulin, and are at high risk of a later gestational diabetes mellitus diagnosis. B Treatment may provide some benefit. E

2.26e Screen for early abnormal glucose metabolism using fasting glucose of 110–125 mg/dL (6.1 mmol/L) or A1C 5.9–6.4% (41–47 mmol/mol). B

General Considerations for Diet Therapy

Recommendation 25

The goals of therapy may be achieved by controlling calorie intake, tailored to maternal and neonatal needs so that the mother can gain proper weight during pregnancy by dividing her meal intake and avoiding long fasting

(Strong recommendation, high-quality evidence).

Question 17

Which diet is appropriate for GDM patients?

Recommendation 26

It is recommended to receive
20% of calorie intake from proteins,
50% from carbohydrates, and
30% from fat with a proper distribution

(Strong recommendation, low-quality evidence).

The diet should include at least three units of low-fat dairy;

the use of more units depends on the energy requirements of the individual

Total carbohydrate intake should be divided into three main courses and three snacks.

Individuals under *insulin therapy* should receive

- ✓ 15% carbohydrate (CHO) in the morning,
- ✓ 10 - 15% CHO in the first snack,
- ✓ 20 - 25% CHO in the lunch meal,
- ✓ 10 - 15% CHO in the second snack,
- ✓ 20 - 25% CHO in the dinner meal,
- ✓ and 15% CHO in the dinner snack (*CHO should be increased for the dinner snack)*

Individuals who are managed *without insulin therapy* should receive

- ✓ 15% CHO in the morning,
- ✓ 10 - 15% CHO in the first snack,
- ✓ 20-25% CHO in the lunch meal,
- ✓ 10-15% CHO in the second snack,
- ✓ 20 - 25% CHO in the dinner meal,
- ✓ and 10% CHO in the dinner snack.

For each 1000 calorie intake, 14 g of fiber should be received, including

- ✓ five units from vegetables,
- ✓ four units from fruits,
- ✓ and one unit from cereals (whole grains mostly).

Simple sugars can account for up to 10% of calorie intake; however, it is more favorable to limit the intake of simple sugars to 5% of calorie intake.

Question 18

Is exercise recommended for women with GDM?

Recommendation 27

Moderate physical activity is recommended for all pregnant women with GDM, and there are no exercise restrictions for controlling blood Glucose

(Strong recommendation, low-quality evidence).

Exercise, if not prohibited during pregnancy, may postpone or resolve the need for pharmacological therapy.

Although aerobic training is more favorable, endurance training may be also helpful.

Moderate-intensity training is recommended for at least 30 minutes daily, four to five days a week.

Women without physical fitness should start physical activity at low intensity (15 minutes daily) and gradually increase the duration of training.

Question 19

What are the goals of therapy to control blood glucose in GDM?

Recommendation 28

The goal of therapy after 24 weeks of gestation is to reach

- FPG < 95 mg/dL,
- one-hour PPG ≤ 140 mg/dL,
- and two-hour PPG ≤ 120 mg/dL

(Strong recommendation, low-quality evidence).

The goals of therapy for GDM women at this stage are not different from those of pregnant women who are diagnosed earlier.

It is *strongly recommended* to reduce the *FPG* level to < 95 mg/dL.

According to *some low-quality evidence*, one-hour plasma glucose ≤ 140 mg/dL and two-hour plasma glucose ≤ 120 mg/dL are recommended.

If recurrent hypoglycemia occurs, higher cutoff points by 5 - 10 mg/dl can be considered for therapeutic goals.

Question 20

How is blood glucose monitored in women with GDM?

Recommendation 29

It is recommended to measure fasting glucose and two-hour PPG levels using a glucometer four times a day, and if not possible, at least 4 - 8 times a week, after achieving the goals of therapy

(Strong recommendation, low-quality evidence).

Question 21

What is the role of HbA1c measurement in the management of GDM?

Recommendation 30

HbA1c may be helpful for glucose monitoring in pregnancy as the second measure after SMBG

(Weak recommendation, low-quality evidence).

In a normal pregnancy, the HbA1c level is lower because of increased red blood cell turnover

It is suggested to maintain HbA1c in pregnancy < 6% if it can be achieved without significant hypoglycemia.

It should be noted that most data on this subject are related to pregnant women with pregestational diabetes

ADA 2022

Glycemic Targets in Pregnancy

15.7 Fasting and postprandial self-monitoring of blood glucose are recommended in both gestational diabetes mellitus and preexisting diabetes in pregnancy to achieve optimal glucose levels.

Glucose targets are fasting plasma glucose <95 mg/dL (5.3 mmol/L) and either 1-h postprandial glucose <140 mg/dL (7.8mmol/L) or 2-hpostprandial glucose <120 mg/dL (6.7 mmol/L).

Some women with preexisting diabetes should also test blood glucose preprandially.

15.8 Due to increased red blood cell turnover, A1C is slightly lower in normal pregnancy than in normal nonpregnant women.

Ideally, the A1C target in pregnancy is <6% (42 mmol/mol) if this can be achieved without significant hypoglycemia, but the target may be relaxed to<7% (53mmol/mol) if necessary to prevent hypoglycemia. B

Glycemic Targets in Pregnancy (continued)

15.9 When used in addition to pre and postprandial self-monitoring of blood glucose, continuous glucose monitoring can help to achieve A1C targets in diabetes and pregnancy. B

15.10 When used in addition to self-monitoring of blood glucose targeting traditional pre- and postprandial targets, continuous glucose monitoring can reduce macrosomia and neonatal hypoglycemia in pregnancy complicated by type 1 diabetes. B

Similar to the targets recommended by ACOG (the same as for GDM), the ADA-recommended targets for women with type 1 or type 2 diabetes are as follows:

- Fasting glucose 70–95 mg/dL (3.9–5.3mmol/L) and either
- One-hour postprandial glucose 110–140 mg/dL (6.1–7.8 mmol/L) or
- Two-hour postprandial glucose 100–120 mg/dL (5.6–6.7 mmol/L)

Question 22

What is the preferred pharmacologic intervention in GDM?

Recommendation 31

Insulin is the drug of choice for women with GDM who cannot meet the therapeutic goals, despite nonpharmacological interventions.

Question 23

What are the indications for oral anti-diabetic agents in GDM?

Recommendation 32

Oral anti-diabetic agents, especially metformin, can be used after 24 weeks of gestation in women with FPG ≤ 110 mg/Dl

(Weak recommendation, moderate-quality evidence).

Metformin is suggested for women with mild GDM (FPG ≤ 110 mg/dL), unwilling to use insulin

However, 30% of these women need to shift to insulin in the next weeks of gestation.

Glibenclamide (glyburide) should be considered as the last option due to the possible increase in

- neonatal hypoglycemia,
- overweight,
- macrosomia

As mentioned earlier, therapy with oral antidiabetic drugs is not recommended during early pregnancy.

Nevertheless, if a pregnant woman is treated with metformin due to other reasons before pregnancy, therapy with metformin can be continued

ADA 2022

Management of Gestational Diabetes Mellitus

15.13 Lifestyle behavior change is an essential component of management of gestational diabetes mellitus and may suffice for the treatment of many women. Insulin should be added if needed to achieve glycemic targets. A

15.14 Insulin is the preferred medication for treating hyperglycemia in gestational diabetes mellitus. Metformin and glyburide should not be used as first-line agents, as both cross the placenta to the fetus. Other oral and noninsulin injectable glucose-lowering medications lack long-term safety data.

15.15 Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester. A

15.16Telehealth visits for pregnant women with GDM improve outcomes compared with standard in person care. A

There are some women with GDM requiring medical therapy who may not be able to use insulin safely or effectively in pregnancy.

Oral agents may be an alternative in these women after a discussion of the known risks and the need or more long term safety data in off-spring.

However, due to the potentialfor growth restriction or acidosis in the setting of placental insufficiency, metformin should not be used in women with hypertension or preeclampsia or at risk for intrauterine growth restriction

Management of Preexisting Type 1 Diabetes and Type 2 Diabetes in Pregnancy

15.17 Insulin should be used for management of type 1 diabetes in pregnancy.Insulin is the preferred agent for the management of type 2 diabetes in pregnancy. B

15.18 Either multiple daily injections or insulin pump technology can be used in pregnancy complicated by type 1 diabetes. C

Preeclampsia and Aspirin

15.19 Women with type 1 or type 2 diabetes should be prescribed low-dose aspirin 100–150 mg/ day starting at 12 to 16 weeks of gestation to lower the risk of preeclampsia. E

A dosage of 162mg/day may be acceptable; currently in the U.S., low-dose aspirin is available in 81-mg tablets. A

a meta-analysis and an additional trial demonstrate that low-dose aspirin <100 mg is not effective in reducing preeclampsia.

Low-dose aspirin >100 mg is required

Pregnancy and Drug Considerations

15.20 In pregnant patients with diabetes and chronic hypertension, a blood pressure target of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension and minimizing impaired fetal growth. E

15.21 Potentially harmful medications in pregnancy (i.e., ACE inhibitors,angiotensin receptor blockers, statins) should be stopped at conception and avoided in sexually active women of childbearing age who are not using reliable contraception. B

Postpartum Recommendations

Question 24

How is a postpartum follow-up in women with GDM?

Recommendation 33

All women with GDM should be evaluated using standard 2-hour 75 g OGTT at 4 - 12 weeks after delivery.

The interpretation of the results is similar to non-pregnant cases

(Strong recommendation, low-quality evidence).

Recommendation 34

In women with normal OGTT after delivery, the annual measurement of FPG is recommended

(Strong recommendation, low-quality evidence).

Recommendation 35

For all prediabetic women diagnosed after delivery, lifestyle modifications (exercise and diet), with or without metformin therapy, are recommended

(Strong recommendation, high-quality evidence).

Gestational diabetes mellitus usually resolves after delivery, as hormones secreted from the placenta, as the main source of insulin resistance, are removed from the body

Therefore, the need for drug therapy mostly resolves after delivery although these patients are at risk of type 2 diabetes, which may occur in 50% of women in the next 20 years

Women who develop GDM at younger gestational ages or those who require a higher insulin dosage are at a higher risk of type 2 diabetes. Therefore, pregnant women with GDM should be followed up after delivery

ADA 2022

Postpartum Care

15.22 Insulin resistance decreases dramatically immediately postpartum, and insulin requirements need to be evaluated and adjusted as they are often roughly half the prepregnancy requirements for the initial few days postpartum. C

Postpartum Care (continued)

15.26 Women with a history of gestational diabetes mellitus should have lifelong screening for the development of type 2 diabetes or prediabetes at least every 1-3 years. B

Technical Remarks Related to OGTT

There is no need for fasting in 50 g OGTT, while other tests require at least eight hours of fasting.

Diet for three days before OGTT should not be constrained (at least 150 g of carbohydrate daily), and physical activity should be done routinely.

Glucose anhydrous (75 g), diluted in water (300 mL), should be used within five minutes;

a cool solution is better tolerated.

Individuals should avoid

- smoking,
- physical activity,
- intake of food, tea, or coffee

during OGTT.

Only outpatient tests should be performed.

The likelihood of false-positive results may increase in inpatients or immobile individuals.

Obstetric care for GDM

Question 25

Which special obstetric care should be considered for women with DM?

Recommendation 36

The fetal viability and gestational age should be confirmed at 7-9 weeks of gestation

(Strong recommendation, high-quality evidence).

Recommendation 37

If GDM is diagnosed before 14 weeks of gestation, and there are additional risk factors e.g:

- history of cardiac malformation in first-degree relatives of the fetus,
- obesity,
- history of GDM

an early detailed anatomy ultrasound is recommended at 11 – 14 weeks of gestation to exclude severe fetal malformations

(Strong recommendation, low-quality evidence).

Recommendation 38

Similar to pregnant women without GDM, the first-trimester screening for chromosomal abnormalities, especially Down syndrome (trisomy 21) and trisomy 18, is recommended between weeks 11 and 14 of gestation.

This type of screening includes nuchal translucency (NT) ultrasound, as well as the measurement of pregnancy-associated plasma protein-A (PAPP-A) and human chorionic gonadotropin (HCG) in the mother's Blood

(Strong recommendation, low-quality evidence).

Gestational diabetes mellitus is associated with an increased risk of maternal and fetal complications both during pregnancy and in the postpartum period.

Screening and identification of these high-risk women are important for improving short- and long-term maternal and fetal outcomes

Question 26

Which fetal health and growth assessments should be performed in women with GDM?

Recommendation 39

An ultrasound monitoring of fetal growth and amniotic fluid volume is recommended for all women with GDM at 28 to 36 weeks of gestation

(weak recommendation, low-quality evidence)

Recommendation 40

Periodic clinical assessments and sonographic growth analysis, if needed, are recommended from the time of diagnosis until term delivery

(Strong recommendation, low-quality evidence).

Recommendation 41

Antenatal fetal testing is usually initiated at 32 weeks of gestation for women with poorly controlled or medication-requiring GDM, without other comorbidities

(Strong recommendation, low-quality evidence)

Recommendation 42

Fetal health tests are recommended at 38 and 39 weeks of gestation

(Strong recommendation, low-quality evidence).

Recommendation 43

Routine monitoring of fetal health using methods, such as

- umbilical arterial Doppler assessment,
- fetal heart rate monitoring,
- biophysical profile test,

before 38 weeks of gestation is not recommended for pregnant women with GDM unless there is a risk of fetal growth restriction

(Strong recommendation, low-quality evidence).

The risk of fetal demise is increased in patients with suboptimal glycemic control.

Hence, fetal surveillance may be valuable in women with poorly controlled GDM.

Since macrosomia and shoulder dystocia are more common in women with GDM, the assessment of fetal growth via ultrasonography or clinical examination in the third trimester is reasonable to detect macrosomia.

There is no consensus regarding antepartum fetal testing in women with well-controlled GDM, who are not medically treated.

If the clinician decides to perform antepartum testing for these patients, it usually begins later than in women with medically treated GDM

Question 27

What are delivery considerations (timing and mode of delivery) for pregnancies complicated by GDM?

Recommendation 44

In women with GDM, controlled with diet and exercise, delivery should not be planned before 39 weeks of gestation, unless otherwise indicated.

In this setting, expectant management up to 41 weeks of gestation, as indicated by antepartum testing, is generally appropriate

(Strong recommendation, high-quality evidence).

Recommendation 45

In women with well-controlled, medically treated GDM, delivery is recommended at 39 to 40 weeks of gestation

(Strong recommendation, low-quality evidence).

Recommendation 46

Delivery between 37 and 39 weeks of gestation may be justified only after incorporating tradeoffs between the risk of prematurity and Stillbirth

(Weak recommendation, low-quality evidence).

Recommendation 47

Late preterm delivery from 34 to 37 weeks of gestation should be performed for women who fail to reach glycemic control even following a hospital admission or those with abnormal antepartum fetal testing results

(Strong recommendation, low-quality evidence).

Recommendation 48

- ✓ The estimated fetal weight < 3800 g at 38 - 39 weeks of gestation,
- ✓ poor glycemic control,
- ✓ poor compliance with treatment,
- ✓ history of stillbirth,
- ✓ cardiovascular diseases

should be considered as *indications for labor induction*

(Strong recommendation, low-quality evidence).

Commonly, women with good glycemic control on treatment do not require delivery before 39 weeks of gestation.

However, the degree of glycemic control requiring earlier delivery and the timing of delivery is not established.

Previous studies suggested the lower incidence of LGA, shoulder dystocia, and cesarean section delivery, besides a higher rate of hyperbilirubinemia, in the group of labor induction at 38 weeks of gestation than in the expectant management group.

Delivery of women with GDM at 38 or 39 weeks of gestation reduces the overall perinatal mortality, without increasing the rate of cesarean section.

However, there is not enough evidence regarding the necessity of cesarean section to reduce the risk of trauma in the setting of suspected macrosomia

Question 28

When is cesarean delivery recommended in GDM?

Recommendation 49

In pregnancies with an estimated fetal weight > 4000 g at 38 - 39 weeks of gestation, elective cesarean section is suggested

(Weak recommendation, low-quality evidence).

Recommendation 50

Glucocorticoids can be used for GDM women to improve lung maturation if premature delivery is suspected or definitely determined

(Weak recommendation, low-quality evidence).

Question 30

What are the considerations for the use of glucocorticoids?

Recommendation 51

In pregnant women under insulin therapy, who require glucocorticoids for fetal lung maturation, the insulin dose should be increased accordingly.

In these cases, hospitalization and blood glucose monitoring are highly recommended

(Strong recommendation, low-quality evidence).

In women with GDM and acceptable glycemic control without insulin therapy, warning about the risk of hyperglycemia and closer monitoring of blood glucose is advisable if glucocorticoid would be prescribed.

Conclusions

The current national GDM guideline was developed to address important clinical issues in the diagnosis and management of Iranian women with GDM.

However, there are still many knowledge gaps in the diagnosis and management of GDM, and there is inadequate information about the short- and long-term maternal and neonatal outcomes related to current practices.

The most important areas of uncertainty include

- GDM diagnostic criteria, especially in the first half of pregnancy,
- the effects of different interventions for dysglycemia on maternal, perinatal, and neonatal outcomes,
- optimal blood sugar thresholds based on the goals of therapy,
- safety and efficacy of oral hypoglycemic medications, especially long-term outcomes.

We believe that the ongoing study by Ramezani et al. may provide suitable answers to most of these uncertainties.

This guideline will be hopefully updated after publishing the results of this national study.


Tnx for attention
And He is the best preserver…