

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

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- 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), 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

- 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 diagnostic criteria , ranging widely from 1.3% to 18.5%

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

Evaluation of Dysglycemia Before Pregnancy

- Who should be assessed for dysglycemia among women contemplating pregnancy?

all non-diabetic women with at least one of the known risk factors must be screened for dysglycemia

Box 1. Risk Factors for Gestational Diabetes Mellitus (GDM)

Risk Factors

1. Previous history of GDM
 2. History of diabetes mellitus in first-degree relatives
 3. Known glucose intolerance
 4. Obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$)
 5. Low physical activity^a
 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
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■ **How** should women at risk for dysglycemia be screened before pregnancy, and what are the diagnostic criteria?

similar to those for **non-pregnant** women

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

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

^bIn the absence of overt hyperglycemia, the diagnosis should be based on two abnormal tests, the same or different tests.

Diabetes Screening in the First Prenatal Visit

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

Fasting plasma glucose must be measured in all women in the first prenatal visit .

the American Diabetes Association, and The American College of Obstetricians and Gynecologists (ACOG) have recommended screening in the first prenatal visits only for women with diabetes risk factors, based on the pre-gestational criteria.

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.

- diagnostic criteria for diabetes in early pregnancy ? In the first prenatal visit

FPG $\geq$ 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 .

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

GDM is diagnosed by an FPG level of 100 - 125 mg/dL, even in one single measurement

.

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

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

^aShould be confirmed with another separate sample test.

- Which **treatment** is used for GDM in early pregnancy?

an **appropriate diet, physical activity, and insulin therapy** if needed.

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.

- **oral antidiabetic agents** is **not recommended** during the **first trimester** of pregnancy.

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

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
two-hour PPG < 120 mg/dL

- the measurement of HbA1c is not recommended for the diagnosis of GDM in Iran

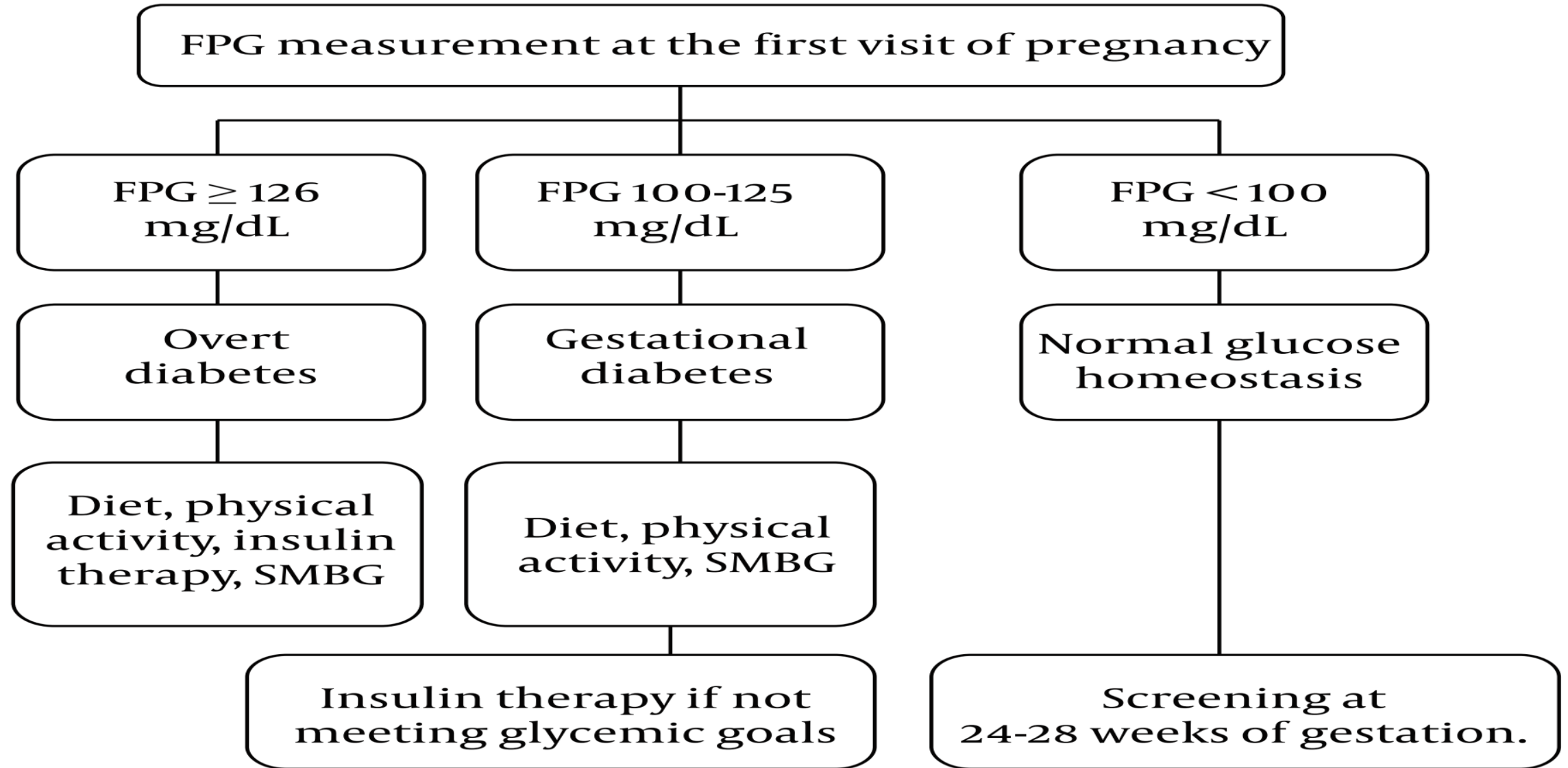


Figure 1. Algorithm for the screening of diabetes at the first visit of pregnancy. Abbreviations: FPG, fasting plasma glucose; SMBG, self-monitoring of blood glucose.

Screening Diabetes in Pregnant Women with Negative First Screening for GDM

- negative screening results (FPG < 100 mg/dL) in earlier evaluations should be screened for GDM at 24 - 28 weeks of gestation
- a two-step glucose tolerance test (GTT) is recommended . There is no consensus regarding the best screening method for GDM due to the lack of outcome-based surveys comparing different methods. The two-step approach, using 50 g of glucose in the first step, is the most common screening approach in many countries.

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

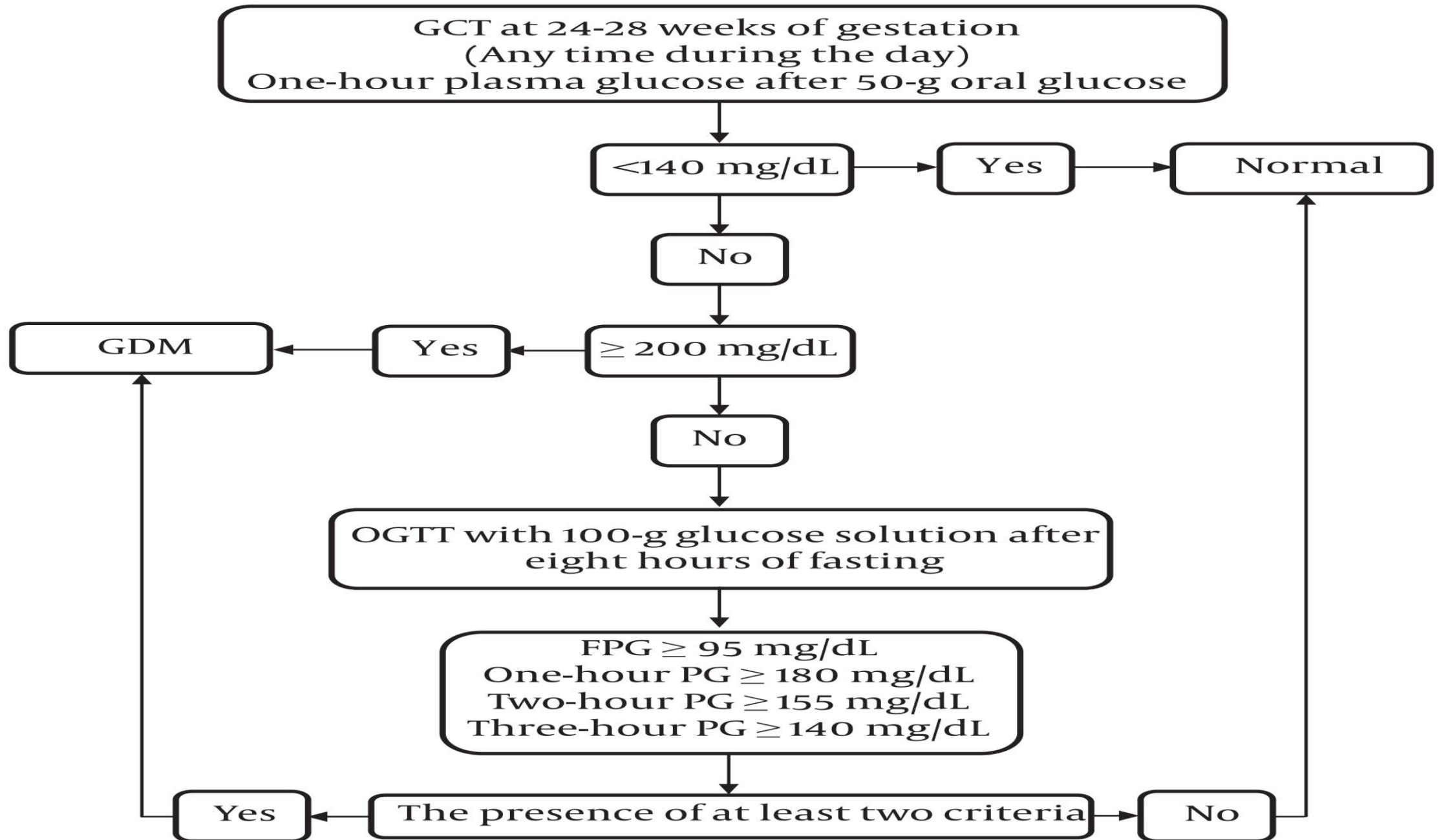
^a100-g oral glucose tolerance test

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	

^aThe diagnosis of GDM is made if at least two of four plasma glucose levels are met or exceeded.

^bOne abnormal value confirms GDM.



- Following the diagnosis of GDM, based on any of the abovementioned guidelines, **repeating GTT is not necessary** .
- If a **prenatal complication** suggestive of GDM (e.g., macrosomia, polyhydramnios, and fetal waist circumference $\geq$ 90th percentile) occurs, GTT should be **repeated** even for women with normal previous evaluations.

Management of GDM

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

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

General Considerations for Diet Therapy:

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.**

■ It is recommended to receive

20% of calorie intake from proteins,
50% from carbohydrates
30% from fat

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

■ Is **exercise** recommended for women with GDM?

Moderate physical activity is recommended , and there are **no exercise restrictions**

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.

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

The goal of therapy after 24 weeks of gestation is not different from those who are diagnosed earlier.

If **recurrent hypoglycemia** occurs, higher **cutoff points by 5 – 10 mg** can be considered .

■ How is blood glucose **monitored** in women with GDM?

**fasting glucose and
two-hour PPG levels**

using a glucometer **four times a day**

if not possible, **at least 4 - 8 times** a week, after achieving the goals of therapy

■

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

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.

- What is the preferred **pharmacologic** intervention in GDM?

Insulin is the drug of **choice** for women with GDM who cannot meet the therapeutic goals, despite non-pharmacological interventions
a week

What are the indications for **oral antidiabetic agents** in GDM?

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, and 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 .

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- 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
- Metformin, when used to treat polycystic ovary syndrome and induce ovulation, should be discontinued by the end of the first trimester
- due to the potential for 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

Postpartum Recommendations

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

2-hour 75 g **OGTT** at **4 - 12 weeks** after delivery.

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

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

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 .

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, and 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

■ 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

- 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.

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

- Antenatal fetal testing is usually initiated at 32 weeks of gestation for women with poorly controlled or medication-requiring GDM, without other comorbidities
- Fetal health tests are recommended at 38 and 39 weeks of gestation
- There is no consensus regarding antepartum fetal testing in women with well-controlled GDM, who are not medically treated.

timing and mode of delivery

- 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

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

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

- 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

- The estimated fetal weight < 3800 g at 38 - 39 weeks of gestation,
 - ✓ poor glycemic control,
 - ✓ poor compliance with treatment,
 - ✓ history of stillbirth,
 - ✓ cardiovascular diseasesshould be considered as indications for labor induction

- When is **cesarean** delivery recommended in GDM?

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

- 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