

# 01

## DIAGNOSIS, CLASSIFICATION AND DESCRIPTION OF GLYCEMIC DISORDERS

### 1. 1 DEFINITION

Diabetes is a chronic metabolic disease caused by absolute insulin deficiency or decreased insulin action which leads to several defects in carbohydrate, fat and protein metabolism. Diabetes requires continuing medical care. Both health care providers and patients should be educated continuously to reduce the risk of acute complications and to prevent chronic, long-term and costly treated sequelae (retinal, renal, neural, and cardiovascular) of the disease.

On the other hand, disglycemia is a qualitative term used to describe other disorders of glucose metabolism.

The recommendations presented here are aimed to reduce the health problems of patients with diabetes in the light of evidence-based medicine and current international consensus.

### 1. 2 DIAGNOSIS AND CLASSIFICATION

The diagnosis and classification of diabetes mellitus and other disorders of glucose metabolism have been changed in the last fifteen years. The International Experts Committee on the Diagnosis and Classification of Diabetes including experts from the American Diabetes Association (ADA) published in 1997 new recommendations for the diagnosis and classification of diabetes, after that in 1999 World Health Organization (WHO) accepted these criteria with a few revisions.

In 2003, ADA has recommended a small revision in definition of impaired fasting glucose (IFG). WHO and International Diabetes Federation (IDF) preserved 1999 criteria in their report published in the late 2006. In contrast, ADA and European Association for the Study of Diabetes (EASD) suggest keeping 2003 revisions unchanged in their last consensus report published in 2007.

#### 1.2.1 Diagnostic Criteria

##### A. Diabetes mellitus

The last diagnostic criteria (arranged in 1997), for diabetes and other disorders of glucose metabolism including 2003 revision are seen in Table 1.1.

Accordingly, diabetes can be diagnosed in three ways. Except conditions with severe diabetes symptoms, diagnosis of diabetes should be confirmed with another method on the following day.

Although standard oral glucose tolerance test (OGTT) with 75 g glucose is more sensitive and specific than fasting plasma glucose (FPG), its routine use is complicated due to high variability from day to day in an individual patient, and being labour-intensive and costly. On the other hand, FPG is commonly used in clinical practice since it is easier to use and cheap. Given the clinical presentation of the disease is more manifest, mostly OGTT is not needed to diagnose type 1 diabetes.

Diagnostic criteria are based on the glucose measurements performed by glucose oxidase method in venous plasma samples. Glucose levels in the whole blood, capillary blood and serum samples, used in clinics or by patients at home to monitor glycemia, are

**Table 1.1 Diagnostic criteria for diabetes mellitus and other disorders of glucose metabolism<sup>†</sup>**

Diabetes mellitus	
Random glucose (plus diabetes symptoms)	≥200 mg/dL
OGTT 2 h PG	≥200 mg/dL
FPG (at least 8 h fasting)	≥126 mg/dL
Impaired glucose tolerance (IGT) <sup>†</sup>	
OGTT 2 h PG	140-199 mg/dL
Impaired fasting glucose (IFG) <sup>†</sup>	
FPG (at least 8 h fasting)	100-125 mg/dL

<sup>†</sup>Blood glucose level is measured by glucose oxidase method in venous plasma as 'mg/dL'.  
<sup>††</sup>In the report by WHO/IDF in 2006, it is stated that the cut-point for normal FPG is 110 mg/dL and the definition of IFG is 110-125 mg/dL.  
 FPG; Fasting plasma glucose, 2 h PG; Two hours plasma glucose, OGTT; Oral glucose tolerance test, IGT; Impaired glucose tolerance, IFG; Impaired fasting glucose, WHO; World Health Organization, IDF; International Diabetes Federation.

slightly lower than plasma levels as shown in the following formulas. Based on these formulas, recently International Federation of Clinical Chemists (IFCC) recommended using devices measuring glucose levels in capillary whole blood samples, after calibrated to PG levels.

According to WHO, postprandial (PP) capillary whole blood glucose levels are equal to venous PG level, however fasting capillary PG levels are considered to be approximately 10% lower than PG levels<sup>††</sup>.

Accordingly, glucose level of 126 mg/dL measured in venous plasma is found 11% less in whole blood (112 mg/dL), 7% less in capillary blood (118 mg/dL) and 5% less in serum (120 mg/dL).

### Haemoglobin A<sub>1c</sub> as a diagnostic test (HbA<sub>1c</sub>: A1C)

The use of glycosylated haemoglobin A1c as a diagnostic test for diabetes has not been recommended for many years because a lack of standardization, and uncertainty of diagnostic threshold. Even though patients who have not been diagnosed diabetes with FPG could be diagnosed with OGTT, however due to standardization problems, A1C might be found in normal range (<6.0%) in these cases. But in recent years raising efforts about the standardization of A1C in all over the world as well as the accumulation evidence of its prognostic importance has raised the question of using A1C as a diagnostic test in diabetes.

Experts Committee on Diabetes, consisted of the representatives of ADA, EASD, IDF and International Federation of Clinical Chemistry (IFCC), has determined the cutoff value of A1C as 6,5% for the diagnosis of diabetes providing that it complies with the international standardization rules on a serial of meetings in 2008. Nevertheless considering A1C is not being performed in every center routinely, having technical problems, lack of standardization, and being costly, the test is not advisable for today to be used as a diagnostic test in our country as in many others.

### B. Gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is defined as a carbohydrate intolerance, with onset or first recognition during pregnancy. The diagnostic criteria for GDM are controversial mainly because lack of correlation to outcome. Many populations use a 3 h 100 g oral glucose tolerance test (OGTT) in all pregnant women who are found to be positive with a 50 g glucose screening test to diagnose GDM. Alternatively a 2 h OGTT with 75 g glucose is also recommended (Table 1.2).

Screening test with 50 g glucose: If PG level, obtained 1 h after a 50 g glucose load, without regard the timing of the last meal, is ≥140 mg/dL at the 24<sup>th</sup> to 28<sup>th</sup> weeks of gestation, it is considered as doubtful for GDM and needs further testing.

Some researchers do not recommend OGTT if 1 h PG after 50 g glucose is >180 mg/dL and advise to follow and treat these cases as GDM.

OGTT with 100 g glucose: If the screening test is positive with 50 g glucose, a 3 h OGTT must be performed to confirm the diagnosis. GDM is diagnosed with at least two values exceeding the upper normal ranges.

OGTT with 75 g glucose: WHO and some authors find it sufficient to perform a 2 h OGTT with 75 g glucose in pregnant women. WHO recommends same evaluation criteria for OGTT in pregnant as it is done in non-pregnant adults.

<sup>†</sup>Plasma glucose (mg/dL) = 0.558 + [20.254 X complete blood glucose (mg/dL) / 18]

Plasma glucose (mg/dL) = 0.102 + [19.295 X capillary blood glucose (mg/dL) / 18]

Plasma glucose (mg/dL) = 0.137 + [18.951 X serum glucose (mg/dL) / 18]

### C. Prediabetes

IGT and IFG, which were previously called as 'borderline diabetes' or 'latent diabetes' are replaced with the term, 'prediabetes'. Both are associated with increased risk of diabetes and cardiovascular diseases as well.

As seen in Table 1.1, it is widely accepted that FPG and OGTT 2 h PG should be 100-125 mg/dL and <140 mg/dL respectively for 'isolated IFG', and FPG <100 mg/dL and 2 h PG 140-199 mg/dL for 'isolated IGT'. However, if both FPG is between 100-125 mg/dL and 2 h PG is between 140-199 mg/dL, the condition is known as 'combined IFG + IGT'. This category indicates further impairments of glucose metabolism. Depending on the fact that few persons with FPG 100-110 mg/dL may have diabetes and that performing OGTT to borderline cases will bring extra costs, WHO and IDF reported in 2006 that the upper limit of FPG should be 110 mg/dL, and IFG description in 1999 has to be kept as 110-125 mg/dL. WHO/IDF report also recommends using the term of "intermediate impairment of glucose metabolism" for IFG and/or IGT categories. On the contrary, in their last consensus report published in 2007 ADA and EASD decided to keep the normal upper level of FPG as 100 mg/dL, and did not change IFG criteria as well as the term of 'prediabetes' used for these disturbances.

International Experts Committee on Diabetes states that people with A1C between 5.7-6.4% are at high risk for diabetes and should be taken into prevention programs. But when considering the lack of standardization, technical difficulties, and high cost, it is not appropriate for our country to use this test to detect high risk people at this point.

**Table 1.2 Diagnosis of GDM based on the ADA and WHO criteria<sup>(\*)</sup>**

	Fasting	1 h	2 h	3 h
<b>ADA criteria</b>				
<b>OGTT with 100 g glucose</b> (≥2 pathological values are diagnostic)	≥95	≥180	≥155	≥140
<b>OGTT with 75 g glucose<sup>(†)</sup></b> (≥2 pathological values are diagnostic)	≥95	≥180	≥155	-
<b>WHO criteria</b>				
<b>OGTT with 75 g glucose</b> (≥1 pathological value is diagnostic)	≥126	-	≥200	-

<sup>(\*)</sup>Blood glucose level is measured by glucose oxidase method in venous plasma as 'mg/dL'. GDM; Gestational diabetes mellitus.  
<sup>(†)</sup>Recently published 'the hyperglycemia and adverse pregnancy outcome study (HAPO)' identified FPG levels, and 1 h and 2 h post glucose (75 g OGTT) PG levels correlated to maternal, perinatal and neonatal outcomes. Accordingly, there is an attempt to reduce thresholds for PG levels (FPG; 92, 1 h PG 180, and 2 h PG 153 mg/dl. 'RG Moses Diabetes Care 2010;33:690-91')

#### SEMT RECOMMENDATIONS FOR THE DIAGNOSIS OF DIABETES

1. FPG should be the main diagnostic test of diabetes.
2. OGTT should be performed in persons at high risk for diabetes mellitus.
3. A 3 h 100 g OGTT should be applied to all pregnant women with a positive 50 g glucose challenge test for definitive diagnosis of GDM.
4. Considering the lack of standardization and high cost, at this moment, A1C is not appropriate in our country to be used for diagnosis of diabetes mellitus.

### 1.2.2 Diabetes Symptoms

The usual symptoms commonly seen in patients with diabetes and rarely seen symptoms of diabetes are listed below.

#### Usual Symptoms

- Polyuria
- Polydipsia
- Polyphagia or loss of appetite
- Weakness and fatigue
- Dry mouth
- Nocturia

#### Rare Symptoms

- Blurred vision
- Unexplained weight loss
- Persistent infections
- Repeated fungal infections
- Pruritus

**SEMT RECOMMENDATIONS**

- In the light of the fact that the lifestyle in our society has changed to increase the risk of diabetes, SEMT recommends keeping 2003 prediabetes criteria in order to raise the awareness about diabetes. According to these criteria normal FPG values should be <100 mg/dL and FPG values of 100-125 mg/dL should be considered as IFG.*
- Considering the lack of standardization and technical difficulties, at this point A1C is not appropriate for our country to be used with this aim.*

**1.2.3 Classification**

Based on the last classification in 1997, there are four clinical types of diabetes as given in Table 1.3. Three of them (type 1 diabetes, type 2 diabetes and GDM) are known as primary, while the other one (specific diabetes types) as secondary forms of diabetes.

**Table 1.3 The aetiological classification of diabetes mellitus**

<b>I. Type 1 diabetes</b> (Generally appeared due to $\beta$ -cell destruction leading to absolute insulin deficiency)	
A. Immune-mediated	
B. Idiopathic	
<b>II. Type 2 diabetes</b> (it is characterized by insulin resistance and impaired insulin secretion)	
<b>III. Gestational diabetes mellitus (GDM)</b> (defined as diabetes mellitus first diagnosed during pregnancy and recovered after delivery)	
<b>IV. Other specific diabetes types</b>	
<p><b>A. Genetic defects of <math>\beta</math>-cell functions (Monogenic forms of diabetes)</b></p> <ul style="list-style-type: none"> <li>Chromosome 20, HNF-4<math>\alpha</math> (MODY1)</li> <li>Chromosome 7, Glucokinase (MODY2)</li> <li>Chromosome 12, HNF-1<math>\alpha</math> (MODY3)</li> <li>Chromosome 13, IPF-1 (MODY4)</li> <li>Chromosome 17, TCF2/HNF-1<math>\beta</math> (MODY5)</li> <li>Chromosome 2, NeuroD1 (MODY6)</li> <li>Chromosome 2, KLF11 (MODY7)</li> <li>Chromosome 9, CEL (MODY8)</li> <li>Chromosome 7, PAX4 (MODY9)</li> <li>Chromosome 11, INS (MODY10)</li> <li>Chromosome 8, BLK (MODY11)</li> <li>Mitochondrial DNA (MTTL1, MTTE, MTTK mutations)</li> <li>Neonatal diabetes (e.g. Kir6.2/KJNC11 mutations)</li> <li>Others</li> </ul> <p><b>B. Genetic defects in insulin action</b></p> <ul style="list-style-type: none"> <li>Leprechaunism</li> <li>Lipomatrophic diabetes</li> <li>Rabson-Mendenhall syndrome</li> <li>Type A insulin resistance</li> <li>Others</li> </ul> <p><b>C. Pancreatic Exocrine Tissue Diseases</b></p> <ul style="list-style-type: none"> <li>Fibrocalculous pancreatopathy</li> <li>Hemochromatosis</li> <li>Cystic fibrosis</li> <li>Neoplasia</li> <li>Pancreatitis</li> <li>Trauma/pancreatectomy</li> <li>Others</li> </ul> <p><b>D. Endocrinopathies</b></p> <ul style="list-style-type: none"> <li>Acromegaly</li> <li>Aldosteronoma</li> <li>Cushing syndrome</li> <li>Foehromocytoma</li> <li>Glucagonoma</li> <li>Hyperthyroidism</li> <li>Somatostatinoma</li> <li>Others</li> </ul>	<p><b>E. Drugs and chemical agents</b></p> <ul style="list-style-type: none"> <li>Atypical anti-physicotic drugs</li> <li>Anti-viral drugs</li> <li><math>\beta</math>-adrenergic agonists</li> <li>Diazoxide</li> <li>Phenytoin</li> <li>Glucocorticoids</li> <li><math>\alpha</math>-interferon</li> <li>Nicotinic acid</li> <li>Pentamidine</li> <li>Protease inhibitors</li> <li>Thiazide diuretics</li> <li>Thyroid hormone</li> <li>Vacor</li> <li>Others</li> </ul> <p><b>G. Uncommon forms of immune-mediated diabetes</b></p> <ul style="list-style-type: none"> <li>Anti-insulin receptor antibodies</li> <li>Stiff-man syndrome</li> <li>Others</li> </ul> <p><b>H. Genetic syndromes associated with diabetes</b> (Other monogenic forms of diabetes)</p> <ul style="list-style-type: none"> <li>Alström syndrome</li> <li>Down syndrome</li> <li>Friedreich's ataxia</li> <li>Huntington's chorea</li> <li>Klinefelter syndrome</li> <li>Laurence-Moon-Biedl syndrome</li> <li>Myotonic dystrophy</li> <li>Porphyria</li> <li>Prader-Willi syndrome</li> <li>Turner syndrome</li> <li>Wolfram (DIDMOAD) syndrome</li> <li>Others</li> </ul>
<p>HNF-1<math>\alpha</math>; hepatocyte nuclear factor-1<math>\alpha</math>, MODY1-11; (maturity onset diabetes of the young 1-11), HNF-4<math>\alpha</math>; hepatocyte nuclear factor-4<math>\alpha</math>, IPF-1; insulin promoter factor-1, HNF-1<math>\beta</math>; hepatocyte nuclear factor-1<math>\beta</math>, TCF2; transcription factor 2, NeuroD1; neurogenic differentiation 1, KLF11; Kruppel like factor 11, CEL; carboxyl ester lipase, PAX4; paired box 4, INS; insulin, BLK; B lymphoid tyrosine kinase, Kir6.2; inwardly rectifying potassium channel 6.2, KCNJ11; potassium channel inwardly rectifying subfamily J member 11, DNA; Deoxy-ribonucleic acid, DIDMOAD syndrome; diabetes mellitus, diabetes insipidus, optic atrophy, deafness (Wolfram syndrome).</p>	

## 1. 3 TYPE 1 DIABETES MELLITUS

### 1.3.1 Pathophysiology and aetiology

There is an absolute insulin deficiency. Approximately 90% of people with type 1 diabetes are positive for islet auto-antibodies causing cell destruction and are deemed to have type 1A while the remaining individuals are negative for auto antibodies and are classified as having type 1B diabetes.

**Type 1A diabetes:** Environmental triggering factors (viruses, toxins, emotional stress) could trigger an autoimmune reaction in genetically-predisposed individuals (with high-risk HLA) to develop progressive  $\beta$ -cell destruction. When 80-90% of  $\beta$ -cells have been destroyed, patients develop clinical symptoms of diabetes. Islet auto antibodies are early markers for type 1A diabetes mellitus.

## 1. 4 TYPE 2 DIABETES MELLITUS

### 1.4.1 Pathophysiology and aetiology

**A. Insulin resistance:** The cells fail to uptake glucose from the blood and turn it into energy due to reduced endogenous insulin action and glucose utilization generating from impaired cell-receptor-postreceptor interactions (there is an intracellular hypoglycemia). The defect in insulin action is seen at the peripheral tissues (primarily muscle, liver and fat tissues). Glucose uptake into muscle and fat cells was reduced.

**B. Reduced insulin secretion:** Pancreas does not release enough insulin in response to increased blood glucose level. The rate of hepatic glucose production is increased. Insulin secretion defect and counter-regulatory factors, reaching the highest rate during morning hours (i.e. cortisol, growth hormone and adrenaline; Dawn phenomenon), are responsible for excessive hepatic glucose production.

Although insulin resistance is generally present for many years before impairment of glucose metabolism are evident and then continued, insulin secretion decreases late in the illness and with complications.

### 1.4.2 Characteristics

- Type 2 diabetes most often occurs after the age of 30, but obesity has led to a dramatic increase in the incidence of type 2 diabetes among children and adolescents within the last 10-15 years.
- Genetic predisposition seems to be the strongest factor. As genetic density increases in the family, next generations are at higher risk of developing the illness, and it presents at a younger age.
- Patients are generally overweight or obese. Body mass index (BMI)  $>25$  kg/m<sup>2</sup>.
- Initially there is no tendency towards DKA, but it presents in late stages following a long term hyperglycemic state and loss of endogenous  $\beta$ -cell reserve.
- It has an insidious onset. Many persons have no history of symptoms.
- Some patients may present with blurred vision, numbness and tingling in hands and feet, foot pain, repeated fungal infections (genitourinary infections in women) and itching.

### 1.4.3 Treatment

- MNT and weight control
- Physical activity
- Oral antidiabetic drugs (OAD) (insulin sensitizers, insulin secretagogues, alpha-glucosidase inhibitors) and insulin, if needed
- SMBG
- Education
- Treatment of comorbidities (hypertension: HT, dyslipidemia etc.) and anti-platelet agents (when needed)

## 1. 5 GESTATIONAL DIABETES MELLITUS (GDM)

### 1.5.1 Pathophysiology and Aetiology

- Insulin resistance due to pregnancy
- Transient diabetes during pregnancy
- Genetic predisposition

### 1.5.2 Characteristics

- Screening tests should be conducted in women at high risk to investigate GDM and gestational glucose intolerance.
- GDM is generally asymptomatic.
- Most of the women with GDM recover to normal glucose levels after delivery, but GDM recurs during the following pregnancies.
- GDM is a significant risk factor for development of permanent type 2 diabetes.

### 1.5.3 Treatment

- Insulin therapy is recommended when MNT and exercise fail to maintain glucose targets. FPG and PP (preferably 1 h or 2 h) PG levels should be controlled (see Chapter 15.3).

#### SEMT RECOMMENDATIONS FOR GESTATIONAL DIABETES

1. FPG and 1 (or 2) h PPPG levels should be used for the follow-up of GDM.
2. If diet and exercise are inadequate to control glucose levels, insulin therapy may become necessary.

## 1.6 INDICATIONS FOR DIABETES SCREENING AND DIAGNOSTIC TESTS

### 1.6.1 Screening for Type 1 Diabetes

- There is no indication for routine screening of type 1 diabetes. However, in many populations family screening for research purposes (autoantibody screening in first degree relatives of patients with type 1 diabetes mellitus) are being performed.
- When marked symptoms and findings exist (polyuria, polydipsia, dry mouth, polyphagia, weight loss, blurred vision, etc.) blood glucose levels should be obtained for diagnosis.

### 1.6.2 Screening for Type 2 Diabetes

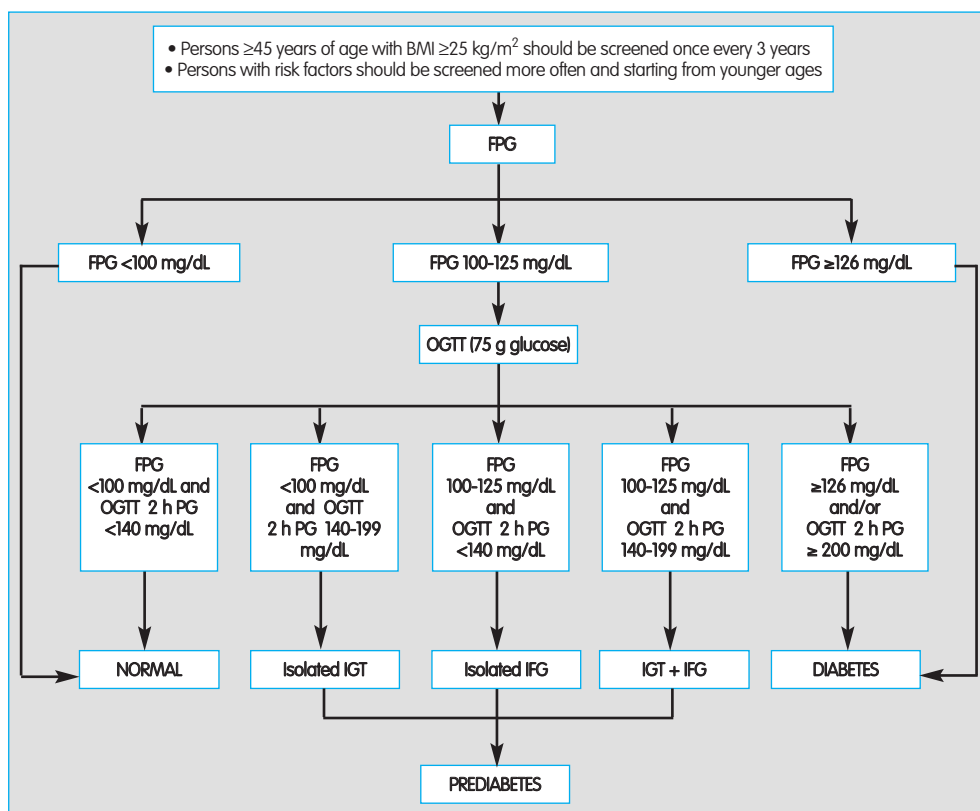
All adults should be evaluated for type 2 diabetes risk factors in accordance with their population-based demographics and clinical features.

- Screening should be conducted once every 3 years, preferably with FPG evaluation, beginning at the age of 45 in overweight/obese persons with a BMI  $\geq 25$  kg/m<sup>2</sup> and particularly in persons with central obesity with waist circumference of over  $\geq 88$  cm for women and  $\geq 102$  cm for men.
- Additionally, peoples belong to at least one of the following risk groups and have BMI  $\geq 25$  kg/m<sup>2</sup> should be screened more often starting from younger ages;
  1. family history of diabetes in a first degree relative
  2. a member of an ethnic group with high diabetes prevalence
  3. previous history of GDM or delivery of a macrosomic infant
  4. hypertension (blood pressure BP  $\geq 140/90$  mmHg)
  5. dyslipidemia (HDL cholesterol  $\leq 35$  mg/dL or triglyceride  $\geq 250$  mg/dL)
  6. previously diagnosed with IFG and/or IGT
  7. women with polycystic ovary syndrome (PCO)
  8. clinical disease or findings related to severe insulin resistance (acanthosis nigricans)
  9. coronary heart disease, cerebrovascular disease or peripheral vascular disease
  10. individuals born with low birth weight
  11. sedentary lifestyle, physical inactivity
  12. high saturated fat and low fiber diet
  13. people with schizophrenia or people treated with antipsychotic drugs

Also, children and adolescents at high risk for diabetes should be screened in every two years beginning at the age of 10. Screening and diagnostic scheme for investigating of type 2 diabetes is shown in Figure 1.1.

**SEMT RECOMMENDATIONS**

1. All adults should be evaluated for type 2 diabetes risk factors in accordance with their demographic and clinical features (Class D, evidence-based on common consensus).
2. FPG should be evaluated in all patients with a BMI  $\geq 25$  kg/m<sup>2</sup> beginning at age 45 (Class D, evidence-based on common consensus).
3. The persons with additional risk factors should be evaluated with FPG and OGTT (if needed) more often, starting from younger ages (Class D, evidence-based on common consensus).
4. OGTT with a 75 g glucose should be performed in patients with FPG 100-125 mg/dL and be evaluated with a 2 h PG levels (Class D, evidence-based on common consensus).



**Figure 1.1 Screening and diagnostic scheme for type 2 diabetes in adults**

BMI: Body mass index, FPG: Fasting plasma glucose, OGTT: Oral glucose tolerance test, 2 h PG: 2-hour plasma glucose, IGT: Impaired glucose tolerance, IFG: Impaired fasting glucose.

### 1.6.3 Gestational diabetes mellitus (GDM)

The risk evaluation should be performed from the first prenatal examination. Pregnant women in the following risk groups are recommended to be tested for diabetes at the beginning of their pregnancy, and negative results are retested in further trimesters.

1. Obesity
2. Previous history of GDM
3. Glycosuria
4. Family history of diabetes in first degree relatives

The current recommendation is to perform screening test between 24<sup>th</sup> and 28<sup>th</sup> weeks of gestation who are not in the high risk group. In Turkish population all pregnant women, whether or not belong to any of the high risk groups, should be screened for GDM between 24<sup>th</sup> and 28<sup>th</sup> weeks of gestation to reduce the risk factors for macrosomia, to control mother's health, and after delivery to prevent permanent type 2 diabetes and insulin resistance.

Alternatively, ADA and some other authorities do not recommend routine screening for low-risk pregnant women. According to this argument, the pregnant women remained in the following groups are considered to be at low-risk for diabetes:

1. Age <25 years
2. Normal body weight before pregnancy
3. Low-risk ethnicity
4. No abnormality of glucose tolerance in the past
5. No prior obstetric adverse outcome

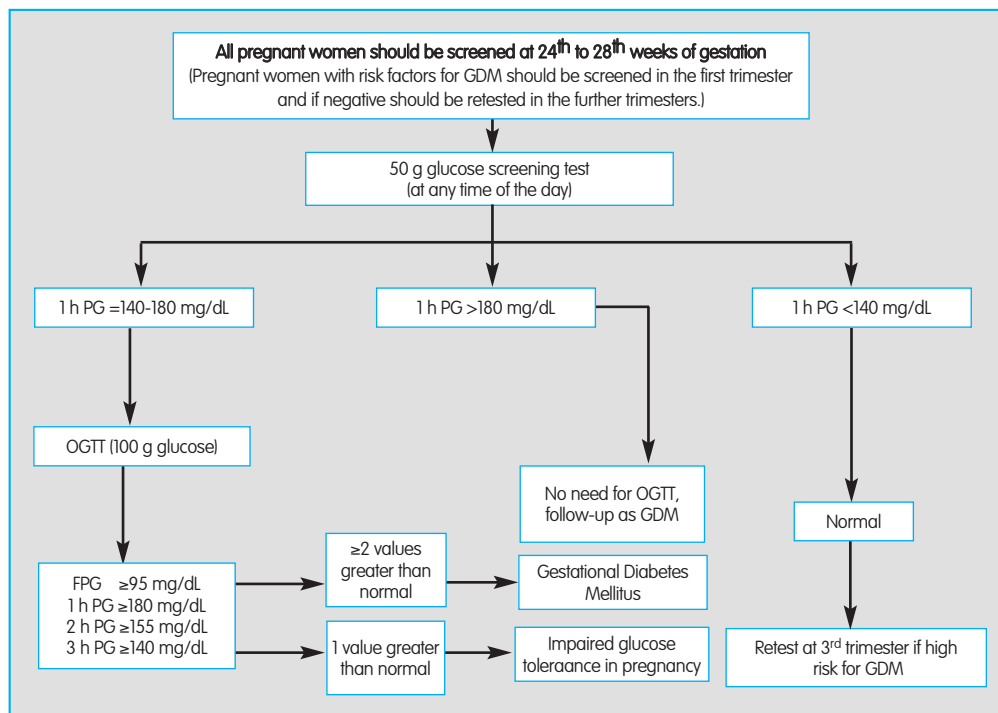
A glucose threshold value >140 mg/dL by measuring PG 1 h after 50 g oral glucose load identifies approximately 80% of women with GDM. However, the yield is further increased to 90% by using a cutoff of >130 mg/dL. Confirmative diagnostic procedures could be established in both conditions.

Those found positive in the screening test with 1 h PG levels 140-180 mg/dL after a 50 g oral glucose administration are subjected to a 3 h 100 g OGTT test to confirm the positive diagnosis. Screening and diagnostic criteria of GDM are summarized in Figure 1.2.

■ If 1 h PG levels are  $\geq 180$  mg/dL on 50 g glucose screening test, OGTT is not required. These women are deemed to have gestational glucose intolerance and monitored as GDM.

■ If there is a high suspicion, 100 g OGTT without any prescreening test is widely accepted.

■ GDM is diagnosed if 2 of 4 PG levels met or exceeded the suggested cutoff values on 3 h 100 g OGTT. Only one glucose level exceeding the cutoff value is considered as gestational glucose intolerance and closely monitored as GDM.



**Figure 1.2 Screening and diagnostic tests for gestational diabetes mellitus<sup>9</sup>**

FPG: Fasting plasma glucose, OGTT: Oral glucose tolerance test, 1 h PG: 1-hour plasma glucose, 2 h PG: 2 hour plasma glucose, 3 h, PG: 3 hour plasma glucose, GDM: Gestational diabetes mellitus.

<sup>9</sup>Recently published 'the hyperglycemia and adverse pregnancy outcome study (HAPO)' identified FPG levels, and 1 h and 2 h post glucose (75 g OGTT) PG levels correlated to maternal, perinatal and neonatal outcomes. Accordingly, there is an attempt to reduce thresholds for PG levels (FPG; 92, 1 h PG 180, and 2 h PG 153 mg/dL. 'RG Moses Diabetes Care 2010;33:690-91).

**SEMT RECOMMENDATIONS**

1. In Turkish population all pregnant women, whether or not at risk, should be screened for GDM in order to reduce fetal morbidity and to predict the future development of type 2 diabetes and insulin resistance among candidate mothers (Class C, Level 3 evidence (1,2)).
2. The vast majority of pregnant women should be screened for GDM between 24th and 28th weeks of gestation (Class D, evidence-based on common consensus).
3. Pregnant women with multiple risk factors for GDM should be tested in the first trimester, and if negative should be retested in the further trimesters (Class D, evidence-based on common consensus).
4. A screening test for GDM is performed by measuring 1 h PG levels after a 50 g oral glucose administration at any time of the day (Class D, Level 4 evidence (3)).
5. Pregnant women found positive at 50 g screening test with 1 h PG 140-180 mg/dL are subject to a 100 g OGTT test to confirm the positive diagnosis.6. If there is a high suspicion for GDM, a diagnostic OGTT is indicated without any prescreening test (Class D, evidence-based on common consensus).
6. If there is a high suspicion for GDM, a diagnostic OGTT is indicated without any prescreening test (Class D, evidence-based on common consensus).
7. If 1 h PG is  $\geq 180$  mg/dL after a 50 g glucose it is not necessary to perform an OGTT. These cases should be followed as GDM.
8. GDM is diagnosed if at least 2 of the 4 PG levels exceeded pre-defined threshold values on a 100 g OGTT (Class D, evidence-based on common consensus);
  - Fasting PG  $\geq 95$  mg/dL
  - 1 h PG  $\geq 180$  mg/dL
  - 2 h PG  $\geq 155$  mg/dL
  - 3 h PG  $\geq 140$  mg/dL

## REFERENCES

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**1.6.4 Preparation for OGTT**

The rules that are considered during OGTT are as follows;

- The patient should consume an unrestricted carbohydrate (CH) diet ( $\geq 150$  g CH daily) and have usual physical activity for at least 3 days before the test.
- The test should be performed after at least an 8 h fasting.
- It is recommended to consume about 30-50 g CH the evening before OGTT.
- During the OGTT, the patient should not eat or drink anything except water. The patients should be advised to refrain from tea, coffee and smoking immediately before or during the procedure.
- The patient is advised to relax and comfortably throughout the test.
- OGTT should not be performed during an acute/chronic infection, if the patient is physically inactive or if there is a treatment with drugs known to impair CH tolerance.
- After fasting blood sample is taken, a standard dose of glucose, 75 g anhydrous glucose (or a 82.5 g glucose monohydrate), dissolved in a 250-300 mL of water is given orally over a 5 minute period.
- Blood sample is drawn 2 h after drinking glucose.
- For children the oral glucose load should be calculated as 1.75 g per kg (maximum 75 g). Plasma samples for glucose concentration are collected in tubes containing sodium fluoride (6 mg per 1 mL blood sample), centrifuged to separate plasma and remained frozen until assayed.

**1.6.5 Other Diagnostic Tests****C-peptide levels**

There is a considerable reserve capacity of  $\beta$ -cells (endogenous insulin) in the pancreas. The routine measurement of this parameter is not necessary in type 1 diabetes mellitus. Fasting and stimulated C-peptide levels can be used to differentiate autoimmune diabetes forms such as LADA from type 2 diabetes, and to detect type 2 diabetes cases who require insulin treatment. However, C-peptide levels may not reflect the actual endogenous insulin reserve due to the effect of glucose toxicity on  $\beta$ -cells during excessive hyperglycemia.

### Islet cell autoantibodies

These are anti-glutamic acid decarboxylase autoantibodies (Anti-GAD), islet cell cytoplasmic antibodies (ICA); insulin autoantibody (IAA) and anti-tyrosine phosphatase antibody (IA2), anti-phogrin antibody (IA2- $\beta$ ), and anti-zinc transporter 8 antibody (Anti-ZnT8). Routine measurement of these autoantibodies is not necessary in type 1 diabetes mellitus. They can be used in differential diagnosis of some autoimmune diabetes forms such as LADA.

#### **SEMT RECOMMENDATIONS**

- *Diabetes in children and non-pregnant women except in high risk individuals for diabetes and suspicious conditions (Class D, evidence-based on common consensus).*
- *A diagnostic OGTT is indicated in high risk peoples for diabetes and suspicious conditions even if FPG is within normal ranges (Class D, evidence-based on common consensus).*
- *Considering technical and standardization problems and being costly, A1C is not advisable for today to be used as a screening and diagnostic test for diabetes.*