Chapter

1

Diagnosis of Diabetes Mellitus

Diabetes mellitus is a major disease which is increasing in the world day-by-day. Uncontrolled diabetes can lead to blindness, limb amputation, kidney failure, and vascular and heart disease. It is a silent disease and can cause lot of complications mentioned above if not diagnosed early. To diagnose diabetes mellitus early, all adults without risk factors should be screened with a test for prediabetes and type 2 diabetes starting at age 35. All women who are planning to become pregnant should be screened for diabetes by doing a fasting glucose test, especially if they have risk factors. For unplanned pregnancies, women should be screened at the first prenatal visit. Screening for gestational diabetes should be done again between 24 and 28 weeks.

ADA (American Diabetes Association) Criteria to Diagnose Diabetes Mellitus:

Diabetes is diagnosed with any one of the following criteria:	
1.	FBS ≥ 126 mg/dL, fasting is defined as no caloric intake for at least 8 hours OR
2.	2 hours post load glucose ≥ 200 mg/dL during an OGTT(oral glucose tolerance test). The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water OR
3.	A1C ≥ 6.5% OR
4.	Random plasma glucose ≥ 200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. Random is defined as anytime of the day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydypsia, and unexplained weight loss

The above tests should be repeated once more to confirm the presence of diabetes mellitus unless there is a clear clinical diagnosis (e.g., patient in a hyperglycemic crisis or with classic symptoms of hyperglycemia and a random plasma glucose ≥ 200 mg/dL). Second test should be done as early as possible without much delay.

OGTT should be performed under controlled conditions to ensure its accuracy. Factors that decrease the value of OGTT include:

1. Carbohydrate restriction (<150 gm for 3 days)
2. Bed rest or severe inactivity
3. Medical or surgical stress
4. Drugs (e.g. Thiazides, steroids, β-blockers, phenytoin)
5. Smoking
6. Anxiety from repeated needle sticks.

Hence, OGTT should not be performed in acutely ill patients. Patients should ideally stop smoking and consume a liberal carbohydrate meal for at least 3 days prior to testing.

CRITERIA TO DIAGNOSE PREDIABETES STATES

"Prediabetes" is the term used for individuals whose glucose levels do not meet the criteria for diabetes but have glucose levels more than the cut-off for normal individuals. These people have abnormal carbohydrate metabolism and are at risk of developing diabetes in future. Prediabetes is diagnosed by the presence of any one of the following criteria.

Impaired fasting glucose (IFG)
Fasting plasma glucose (FPG) 100 mg/dL to 125 mg/dL OR
Impaired glucose tolerance (IGT)
2 h plasma glucoe during 75 g OGTT 140 mg/dL to 199 mg/dL OR
A1C 5.7–6.4%

All patients with prediabetes states should be treated with diet and exercise and should be followed up yearly for the progression to diabetes.

Classification of Diabetes Mellitus

The ADA classification of diabetes includes four clinical classes:

- Type 1 diabetes (results from β-cell destruction, usually leading to absolute insulin deficiency).
- Type 2 diabetes (results from a progressive insulin secretory defect on the background of insulin resistance).
- Other specific types of diabetes due to other causes, e.g., genetic defects in β-cell function, genetic defects in insulin action, diseases of the exocrine pancreas (such as cystic fibrosis), and drug or chemical induced (such as in the treatment of AIDS or after organ transplantation).
- Gestational diabetes mellitus (GDM) (diagnosed during pregnancy).

How to Know the Type of Diabetes

Understanding the type of diabetes is important from treatment point of view. However, many people do not fit exactly into one type. For example, some people with type 1 diabetes may become obese and develop insulin resistance which is a feature of type 2 diabetes. On the other hand most type 2 diabetics in advanced stages have little or no endogenous insulin secretion and such people have the characteristics of type 1 diabetes. Blurring of the lines between type 1 and type 2 diabetes is increasingly becoming common.

Clinical Clues

Type 1 diabetes usually begins in childhood, but can occur at any age. Approximately 50% of the adults develop type 1 diabetes before the age 40 years. The remainders develop it as older adults. Presence of other autoimmune diseases like celiac disease, Graves' disease, hypothyroidism, Addisons disease, pernicious anemia, etc. suggests type 1 diabetes. Family history of type 1 diabetes again suggests type 1 diabetes in the patient. Persons with type 1 diabetes are usually thin and have very high blood sugars at presentation. They often present with diabetic ketoacidosis. A type 2 diabetic is usually obese, presents after 35 years of age and may satisfy the criteria of metabolic syndrome. If the person is on oral antidiabetic agents

and is controlled with it, then he has type 2 diabetes because obviously oral agents do not work in type 1 diabetes.

Laboratory Clues

Ketone bodies: Presence of a large amount of ketone bodies goes in favour of type 1 diabetes, though type 2 also can have ketone bodies. If insulin is injected before testing for ketone bodies, the opportunity to find a large amounts of ketone bodies may be missed.

C- peptide levels: C-peptide is half of the precursor molecule to insulin that is split off when insulin is produced from the body. C-peptide levels can reveal how much insulin a person is producing. If c-peptide level is normal or high, type 2 diabetes is likely. If significantly low type 1 diabetes is likely. If the level is low normal, the person may have early type 1 or longstanding type 2 DM. When external insulin is being used it may suppress endogenous insulin production and hence c-peptide levels may be low. C-peptide levels should be measured after insulin has been reduced or discontinued, and the blood sugar has risen to 200 mg/dL or more.

Antibodies: Type 1 diabetes is an autoimmune disease, hence anti-islet anti-bodies and anti-GAD 65 (glutamic acid decorboxylase) antibodies can be found in 80 – 90% of patients with type 1 diabetes. Anti-GAD 65 antibodies can be found in only 3% of normal population. When both islet cell and GAD 65 antibodies are detected they increase the autoimmune disease detection to >90%. Blood tests can be done to detect the presence of these antibodies. If the person does not already have diabetes, presence of these antibodies predicts development of type 1 diabetes in such persons.

High triglyceride, low HDL, high uric acid: All these are markers of metabolic syndrome and suggest type 2 diabetes.

Glucose clamp procedure to detect insulin resistance: This is the gold standard to detect insulin resistance. Insulin resistance suggests type 2 diabetes. However, this is a time consuming procedure and is used only in research settings.

All the above lab tests especially C-peptide levels and auto antibodies need not be done routinely. Use them only when

a person's diabetes type is not clear or when treatment is not working for unknown reasons.

Glycemic Targets for Adults with Diabetes as per American Diabetes Association (ADA):

A1C	***< 7.0%***
Preprandial capillary plasma glucose	80 – 130 mg/dL (4.4 to 7.2 mmol/l)
Peak postprandial capillary plasma glucose	< 180 mg/dL (< 10.0 mmol/l)

Blood Pressure Targets

For individuals with diabetes and hypertension at higher CV risk, a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained.

For individuals with diabetes and hypertension at lower risk for CVD a target blood pressure of <140/90 mmHg is acceptable.

Lipid Targets

2018 AHA/ACC/Guideline on the management of blood cholesterol recommends treatment with a statin for 4 groups of patients, comprised of those with any of the following:

- Clinical ASCVD (atherosclerotic cardiovascular disease)
- LDL cholesterol ≥ 190 mg/dL
- Age 40 to 75, with diabetes and LDL cholesterol 70 to 189 mg/dL
- Age 40 to 75, LDL cholesterol 70 to 189 mg/dL, and estimated 10-year risk of ASCVD ≥ 7.5%

For primary prevention, statin therapy should lower LDL-C approximately 30% to more than 50%.

For secondary prevention, as defined by a patient who has coronary artery disease, a target goal is set for LDL-C less than 70 mg/dL.

If the patient is a high risk (already had acute coronary syndrome in the last year, familial hypercholesterolemia, diabetes, chronic kidney disease (stage 3 or 4), or atherosclerotic cardiovascular disease event, or the need for revascularization while on a statin), then the LDL goal should be less than 50.

A1C Level

- A1C is the primary tool for assessing glycemic control and has a strong predictive value for diabetes complications. The A1C goal *for patients in general* is <7%. TheA1C goal *for the individual patient* is as close to normal (<6%) as possible without significant hypoglycemia.
- An A1C goal for many nonpregnant adults of <7% (53 mmol/mol) without significant hypoglycemia is appropriate.
- On the basis of provider judgment and patient preference, achievement of lower A1C levels than the goal of 7% may be acceptable and even beneficial if it can be achieved safely without significant hypoglycemia or other adverse effects of treatment.
- Less stringent A1C goals (such as <8%) may be appropriate for patients with limited life expectancy or where the harms of treatment are greater than the benefits.
- Less stringent treatment goals may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancy, very young children or older adults, and individuals with comorbid conditions.
- Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness, perioperatively, following myocardial infarction, and in pregnancy.
- Goals should be individualized
- Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals

A1C Testing Recommendations

- Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control).
- Perform the A1C test once in 3 months in patients whose therapy has changed or who are not meeting glycemic goals.
- Use of point-of-care testing for A1C allows for timely decision on therapy changes, when needed.