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Diabetes Mellitus

Types, Diagnostics and Therapy

OAD and Insulin Protocols





Ravi N Humbarwadi

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CHAPTER 3

Blood Glucose Levels

INTRODUCTION

Blood tests can confirm the diagnosis of diabetes. While fasting blood sugar (FBS) and glycosylated hemoglobin (HbA1c) can confirm diabetes and prediabetes, random blood sugar (RBS) levels are only indicative of diabetes **(Table 1)**. Two abnormal results are needed to confirm the diagnosis.

While HbA1c has some benefits such as no fasting and low day-to-day variance, it can be affected by certain drugs used in human immunodeficiency virus (HIV), glucose-6-phosphate dehydrogenase (G6PD) deficiency, pregnancy (second and third trimesters), hemodialysis, and sickle cell anemia wherein FBS is preferred. Any marked difference in HbA1c and FBS should raise suspicion of the tests' results.

HbA1c levels:

- *Normal*: Below 5.7%
- *Prediabetic*: 5.7–6.4%
- *Diabetic*: 6.5% or higher on two separate tests

FBS levels: Blood sample is drawn in the morning before breakfast with at least 8 hours of fasting.

- *Normal*: 70–100 mg/dL
- *Prediabetic*: 100 and 125 mg/dL
- *Diabetic*: 126 mg/dL or higher

TABLE 1: Blood glucose levels for diagnosis of diabetes mellitus.

Laboratory test	Normal range	Prediabetic	Diabetes
Fasting blood glucose (FBG)	70–100 mg/dL 5.5 mmol/L	100–125 mg/dL 5.5–6.9 mmol/L	Above 126 mg/dL 7 mmol/L
2-hour postprandial	Below 140 mg/dL 7.8 mmol/L	140–199 mg/dL 7.8–11 mmol/L	Above 200 mg/dL 11 mmol/L
Random blood sugar (RBS)	Below 200 mg/dL 11 mmol/L	N/A	Above 200 mg/dL 11 mmol/L

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ORAL GLUCOSE TOLERANCE TESTS

- Blood sample is drawn in the morning before breakfast with at least 8–12 hours of fasting.
- After the first baseline sample is drawn, the patient is given a glucose solution to drink.
- After 2 hours another blood sample is drawn.

Results

- Baseline sample results are assessed as per FBS levels.
- Two hours after drinking the glucose solution:
  - *Normal*: <140 mg/dL (7.8 mmol/L)
  - *Impaired glucose tolerance* (*IGT*): 140–199 mg/dL (7.8 and 11 mmol/L)
  - *Diabetes*: 200 mg/dL or higher and 11 mmol/L or higher

Patients with IGT and impaired fasting glycemia (IFG) are considered to be in the prediabetic range and can potentially progress to type 2 diabetes mellitus (T2DM).

Oral glucose tolerance test (OGTT) is generally used only during pregnancy. Due to the long time taken to do the test, it is now practically not used other than during pregnancy.

The American College of Obstetricians and Gynecologists (ACOG) recommends a 1-hour blood glucose challenge test to screen for gestational diabetes in low-risk pregnant women between 24 and 28 weeks of pregnancy.

GLUCOSE SCREENING TESTS DURING PREGNANCY

A glucose screening test is a routine test during pregnancy that checks the blood glucose level.

One-step Test

You need to go to the laboratory only once for a 2-hour glucose tolerance test.

For this test:

- Do not eat or drink anything (other than sips of water) for 8–12 hours before your test. (You also cannot eat during the test).
- The patient has to drink a solution having 75 g of glucose.
- Blood is tested before drinking the liquid and three more times after drinking at intervals of 60 minutes. Every time, the blood glucose level test will be done.

A diagnosis of gestational diabetes mellitus is made if at least one of these glucose levels is elevated:

- *Fasting*: ≥92 mg/dL (5.1 mmol/L)
- *1-hour*: ≥180 mg/dL (10 mmol/L)
- *2-hour*: ≥153 mg/dL (8.5 mmol/L)

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Two-step Test

First step: Glucose screening test (1-hour test)
- No need to restrict diet.
- The patient has to drink a 50 g glucose solution.
- Blood is tested after 1 hour.

After 1 hour:
- *140 mg/dL or lower*: Normal
- *More than 140 mg/dL*: Glucose tolerance test will be done
- *More than 190 mg/dL (10.6 mmol/L)*: Gestational diabetes

Second step: Glucose tolerance test (3-hour test).
- Do not eat or drink anything (other than water) for 8–12 hours before the test (Do not eat during the test).
- The patient is given to drink 100 g of glucose.
- Blood tested before drinking the liquid and three more times after drinking at intervals of 60 minutes. Every time, the blood glucose level test will be done.

After 1 hour: <180 mg/dL (10 mmol/L)

After 2 hours: <155 mg/dL (8.6 mmol/L)

After 3 hours: <140 mg/dL (7.8 mmol/L)

If one of the results is higher, the patient may be advised to test again in 4 weeks. If two are higher, then gestational diabetes is diagnosed.

Target blood sugar levels for women during pregnancy:
- *Before a meal*: <95 mg/dL
- *1 hour after a meal*: <140 mg/dL
- *2 hours after a meal*: <120 mg/dL

TYPE 1 DIABETES MELLITUS

Type 1 diabetes mellitus (T1DM) commonly presents as polyuria or polydipsia. It may also present with flu-like symptoms. Medics should have a high degree of suspicion when patients have other associated diabetic symptoms especially in the age-specific population. Appropriate investigations need to be done. The most common age at diagnosis is 4–6 years and in early teenage is 10–14 years.

These symptoms may appear suddenly:
- Feeling thirsty
- Feeling very hungry
- Urinating frequently
- Bed-wetting in kids with an unusually higher severity
- Losing weight noticeably

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However, T1DM can also present as diabetic ketoacidosis (DKA). A fruity odor breath due to high ketone levels in the blood as a result of muscle and fat breakdown, heavy breathing, and vomiting are typical of DKA. T1DM are prone to DKA which can progress to loss of consciousness and can even be fatal if not treated on emergent basis.

Risk Factors

- Family history of autoimmune diseases such as hypothyroidism, hyperthyroidism, or celiac sprue
- Persisting hyperglycemia despite treatment for T2DM
- Without a family history of T2DM but having diabetic symptoms

To conclude, the patient of T1DM may present with acute symptoms, and significantly elevated blood glucose levels, and nearly one-third present with DKA.

The next step is doing blood tests to confirm.

Random Blood Glucose Test

This test measures a patient's current blood sugar regardless of duration of when the person had last eaten. This may be the first test since it gives an overview of the blood glucose status in quick time. The doctor may then ask for other tests which are more accurate.

Fasting Blood Glucose Test

A fasting blood glucose test is done when T1DM is suspected. This is done in the morning after overnight fasting.

Oral Glucose Tolerance Test

After fasting and having an initial blood test, the patient is given a sugary drink. The blood sugar is tested again after 2 hours. This measures the response to carbohydrate intake.

Glycosylated Hemoglobin Test

This blood test shows the average blood sugar level for the past 3 months.

Tests Specific to Type 1 Diabetes Mellitus

- *C-peptide*: C-peptide and insulin levels are low in T1DM; C-peptide mirrors the level of naturally produced insulin in the body.
- *Insulin autoantibodies (IAA)*: Levels of antibodies targeting insulin
- *Insulinoma-associated-2 autoantibodies (IA-2A)*: Levels of antibodies against a specific enzyme in beta cells
- *Zinc transporter 8 autoantibody (ZnT8Ab)*: Levels of antibodies targeting an enzyme that is specific to beta cells

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- *Islet cell cytoplasmic autoantibodies (ICA)*: Levels of type of islet cell antibodies present in up to 80% of people with T1DM.
- *Glutamic acid decarboxylase autoantibodies (GADA)/anti-glutamic acid decarboxylase (anti-GAD)*: Levels of antibodies against a specific enzyme in the beta cells

Even without elevated glucose levels, presence of two or more autoantibodies are strong predictors of future hyperglycemia or T1DM.

When diagnosed with diabetes, a ZnT8Ab test is done. This will be positive for T1DM.

The C-peptide test, ZnT8Ab, IA-2A, and anti-GAD tests are common antibody tests done to confirm T1DM.

NORMAL C-PEPTIDE

- 0.5–2.0 ng/mL
- 0.2–0.8 nmol/L

C-*peptide level of <0.2 nmol/L*: T1DM

In practice, doctors may use C-peptide for two reasons:
1. To support the distinction between T1DM or T2DM
2. To find out how much insulin the pancreas still makes

C-peptide levels directly correlate to insulin levels produced by the pancreas. The lower the level of C-peptide, lower the endogenous insulin.

High level of C-peptide indicates higher levels of insulin: T2DM, a kidney problem or an insulinoma, a tumor of the insulin-making cells in the pancreas. **Box 1** shows the uses of diagnostic C-peptide test.

THE HONEYMOON PHASE

During the "honeymoon phase", patients with T1DM are asymptomatic for a few months to a year. The injected insulin takes care of the need of the body and also takes the stress off the pancreatic beta cells which then allows the B cells to produce insulin. However, the majority of the insulin-producing beta cells eventually stop functioning and then symptoms begin to appear.

No matter how good HbA1c or blood sugar tests are during the honeymoon phase, the disease is still present. During this phase, doctors maintain blood glucose with low-dose insulin. After the remaining beta cells are finally destroyed, insulin dose will be increased.

BOX 1: Diagnostic C-peptide test.

- Differentiate between T1DM or T2DM
- Diagnostic test for MODY, in addition to other tests
- Diagnostic test for LADA, in addition to antibody testing

(LADA: latent autoimmune diabetes in adults; MODY: maturity-onset diabetes of the young; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus)

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LATENT AUTOIMMUNE DIABETES IN ADULTS

Latent autoimmune diabetes in adults (LADA) is a slow-progressing form of autoimmune diabetes. Insulin production is gradually stopped due to slow damage to the pancreatic beta cells.

Features

- Lack of metabolic syndrome characteristics such as obesity, high cholesterol, and high blood pressure.
- Uncontrolled hyperglycemia despite using oral drugs
- Lower age at onset, lower body mass index (BMI) and more frequent insulin injections than T2DM.
- LADA patients have worse HbA1c levels than T2DM patients.

Antibody testing and C peptide levels help diagnose LADA. Anti-GAD test is the most common method. However, in the very early stages of LADA, it is possible that there may be no detectable antibodies in some patients.

DIAGNOSIS OF DIABETES

- Random blood sugar of 200 mg/dL (11.1 mmol/L) or more along with symptoms
- FBS of 126 mg/dL (7 mmol/L) or more
- HbA1c of 6.5% (48 mmol/mol) or more

If any of the tests are positive, a repeat test is done and then only diabetes is confirmed. FBS and HbA1c are the preferred and commonly used diagnostic tests to confirm diabetes.

SCREENING

The American Diabetes Association (ADA) recommends routine screening for T2DM.

- In adults aged more than 35 years
- People younger than 35 years who are overweight and with at least one risk factor
- Women with history of gestational diabetes
- In prediabetics
- Overweight children with family history of T2DM or any other risk factor

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Diabetes Mellitus

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Salient Features

- This is an essential handbook for students and reference book for clinicians.
- Consider a patient who comes to the clinic. Right from presentation, diagnostic confirmation, initial therapy, choice of combination with oral antidiabetic drug, and finally insulin protocols—all these are described in a concise yet comprehensive manner
- A step-wise approach takes the medic from diagnosis to therapy
- Includes 5 Case Studies
- Based on international standard of care and encompasses the latest guidelines
- Oral antidiabetic drug and insulin are dealt with in detail and hence this book straddles both medical and pharma domains.

Ravi N Humbarwadi is working in the drug safety domain. He has been associated with Apollo Hospitals group, Manipal, and Mphasis in various capacities. While with Mphasis, he was selected for training in critical illness risk assessment in Glasgow, Scotland. He has been writing on various wide-ranging medical topics including oncology and cardiology. His drug safety books have sold in 18 countries. Known for bringing the latest information and presenting in a simple, easy-to-remember format, his books are popular with students as well as professionals.

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