

1. Diabetes Mellitus

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1.1 Introduction:

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia. Early diagnosis and optimal management utilizing the recommended laboratory tests is required to prevent the metabolic, microvascular and macrovascular complications of the disease.

Impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT) are both states of impaired glucose regulation and carry the risk of development of future diabetes. IFG is determined by the Fasting Plasma glucose (FPG) measurement whilst IGT is determined by the 2hr value of an oral glucose tolerance test (OGTT). Early identification of these states in individuals, and management with life style modifications, and appropriate pharmacotherapy will prevent them progressing to diabetes as well as reduce associated cardiovascular risks.

These guidelines are for the doctors and nursing officers involved in the management of patients with DM as well as for the doctors, biochemists and medical laboratory technologists of the pathology laboratories.

1.2 Methodology:

Published evidence based current international guidelines for laboratory analysis for the diagnosis and management of DM were reviewed. The following recommendations are being made based on those with adaptations to suit infrastructure and the facilities available at the State Sector hospitals.

1.3 Laboratory tests for Screening and Diagnosis of DM:

Laboratory tests for screening and diagnosis of DM

- Fasting plasma glucose (FPG)
- Random plasma glucose (RPG)
- 2hr plasma glucose of an OGTT (2hr PG)
- Capillary blood Glucose (CBG)
- Urinary glucose (UG)

TH/GH/BH	DH/PU
<ul style="list-style-type: none"> • Fasting plasma glucose (FPG) • Random plasma glucose (RPG) • 2hr plasma glucose of an OGTT (2hr PG) • Capillary blood Glucose (CBG) • Urinary glucose (UG) 	<ul style="list-style-type: none"> • Capillary blood Glucose (CBG) • Urinary glucose (UG)

1.3.1 Screening:

- **Screening** is recommended for all individuals with one or more major risk factors for developing DM. (Grade X)
- FPG is the laboratory test recommended for screening of individuals for DM. (Grade X)
- RPG is an alternative test for screening. (Grade X)
- When facilities to do FPG or RPG are not available, CBG and UG are alternatives for

screening for patients with classical symptoms of DM. (Grade X)

Major Risk factors for developing DM (type 2)

- Age \geq 45 years
- Overweight (BMI \geq 25 kg/m²)
- Family history of DM (parents or siblings)
- Habitual physical inactivity
- Previously identified IFG or IGT
- Hypertension (\geq 140/90 mmHg in adults)
- HDL cholesterol $<$ 35 mg/dl (0.09 mmol/L) and or TG $>$ 250 mg/dl (2.82 mmol/L)
- History of vascular disease (Coronary artery disease, cerebrovascular disease or peripheral vascular disease)
- History of GDM or delivery of a baby weighing $>$ 9 lbs
- Polycystic ovary syndrome

1.3.2 Diagnosis:

- The term diagnosis refers to confirmation of diabetes in people who have symptoms, or who have had a positive screening test.
- Either FPG or RPG can be used for the confirmation of diagnosis.

- In symptomatic individuals one abnormal plasma glucose measurement in the diabetic range confirms the diagnosis.
- Asymptomatic individuals with a positive screening test (FPG or RPG) need another abnormal plasma glucose measurement on another day for the confirmation of the diagnosis.
- OGTT is not recommended for routine use as a confirmatory test.

1.4 Indications for OGTT:

In non pregnant adults an OGTT is recommended,

- for all patients with IFG.
- When results of the recommended diagnostic tests (FPG and RPG) fail to determine the diagnosis in an individual patient (E.g. equivocal or borderline results).

1.5 Criteria for the diagnosis of Diabetes Mellitus:

Criteria for the diagnosis of diabetes mellitus

- A. FPG ≥ 7.0 mmol/l (126 mg/dl).
Fasting is defined as no caloric intake for at least 8 h.
or
- B. Symptoms of diabetes plus random plasma glucose concentration ≥ 11.1 mmol/l (200 mg/dl).
Random is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.
or
- C. 2-h postload glucose ≥ 11.1 mmol/l (200 mg/dl) during an OGTT.

1.6 Interpretation of results for diagnostic tests (FPG, RPG and 2hr PG)

	Normal	IFG	IGT	DM
FPG mmol/L (mg/dL)	<5.6 (<100)	≥ 5.6, ≤ 6.9 (≥ 100, ≤ 125)	<7.0 (<126)	≥ 7.0 (≥126)
RPG mmol/L (mg/dL)	< 5.6 (<100)	N/A	N/A	≥ 11.1 (≥200)
2 hr PG mmol/L(mg/dL)	< 7.8 (<140)	N/A	≥7.8 (≥140)	≥ 11.1 (≥200)

1.7 Baseline laboratory tests in a newly diagnosed patient with DM:

Patients with type 2 DM could have had the disease for 5 – 7 years prior to the diagnosis.

Therefore the following biochemical tests are recommended for all newly diagnosed patients with DM to detect other associated metabolic and microvascular complications. **(Grade X)**

Baseline biochemical tests for newly diagnosed patients with DM

- Serum electrolytes
- Serum creatinine and estimated GFR (eGFR)
- Lipid profile (preferred) or serum cholesterol
- Urinary protein
- Urinary microalbumin (patients with negative proteinuria)
- 24 hr urinary protein (patients with overt proteinuria)

1.8 Laboratory tests for the follow up of patients with IFG, IGT and DM (impaired glucose regulation and diabetes):

- All patients with IFG alone should be followed up with FPG annually. **(Grade X)**
- All patients with IGT should be followed up with an OGTT annually. **(Grade X)**

- Patients diagnosed with DM should be monitored with FPG monthly. (Grade X)
- Glycosylated Haemoglobin (HbA_{1C}) is recommended for follow up once in three months until satisfactory glycaemic control is achieved. (Grade Y)
- HbA_{1C} is recommended at least once in six months in patients who have achieved optimal control. (Grade Y)
- Annual microalbumin (patients with negative proteinuria) and lipid profile testing are recommended for patients with DM. (Grade Y)

1.9 Laboratory tests in the management of patients with metabolic complications of DM:

Metabolic complications of DM

- Diabetic ketoacidotic coma
- Hyperosmolar nonketotic coma
- Hypoglycaemia

Recommended laboratory tests in patients with metabolic complications

- Capillary Blood glucose (Grade X)
- Random plasma glucose (If CBG is abnormal) (Grade X)
- Urinary glucose (Grade X)
- Urinary ketone bodies (Grade X)
- Serum electrolytes (Grade X)
- Blood urea (Grade X)
- Serum creatinine (Grade Y)
- Arterial blood gas analysis (Grade Y)

TH/GH/BH	DH/PU
<ul style="list-style-type: none"> • Capillary Blood glucose (Grade X) • Random plasma glucose (If CBG is abnormal) (Grade X) • Urinary glucose (Grade X) • Urinary ketone bodies (Grade X) • Serum electrolytes (Grade X) • Blood urea (Grade X) • Serum creatinine (Grade Y) • Arterial blood gas analysis (Grade Y) 	<ul style="list-style-type: none"> • Capillary blood Glucose (CBG) (Grade X) • Urinary glucose (UG) (Grade X) • Urinary ketone bodies (Grade X)

1.10 Laboratory tests for Screening, Diagnosis and Management of Gestational DM:

Selective screening is recommended for women with risk factors for developing GDM. (Grade X)

Risk factors for GDM

- Glycosuria in the 1st trimester
- Glycosuria on two occasions in either the second or third trimester
- Polyhydroamnios, macrosomia, large for gestational age in the current pregnancy
- Previous unexplained stillbirth
- Family history in a first degree relative
- Obesity (BMI>25Kg/m²) at the booking visit
- Age > 35 years
- Previous GDM
- Recurrent miscarriages
- Previous macrosomic baby

- A. 2hr postprandial plasma glucose (2hr PPG) following a standard meal at antenatal booking is recommended for screening for GDM. (Grade X)
- B. All abnormal screening tests should be followed up with an OGTT for confirmation of GDM. (Grade X)
- C. Pregnant mothers with a negative screening test should be evaluated at 24 -28 weeks of gestation with an OGTT. (Grade X)
- D. Protocol for OGTT is the same as for non pregnant adults and should be interpreted by an Obstetrician. (Grade X)

1.11 Notes on sample collection and transport:

1.11.1 FPG /RPG/2hr PG

- Venous plasma is recommended. (Grade X)
- 1 or 2 ml of blood should be drawn as required by the pathology laboratory of the hospital.
- Blood should be collected to a container or tube with Sodium Fluoride (Inhibitor of glycolysis) and Potassium Oxalate (anticoagulant).(GradeX)
- 0.1ml of Sodium Fluoride (1g) and potassium oxalate (3g) mixture in 100 ml of distilled water for 1ml of blood is recommended.
- 2ml of venous blood should be collected to a plain bottle or tube for serum electrolytes, blood urea, serum creatinine, serum cholesterol, and 5 ml for lipid profile.
- 2ml of venous blood should be collected to a bottle or tube with EDTA for HbA_{1c}.
- Fresh mid stream urine samples should be collected into clean, dry, screw capped containers for urinary glucose, ketone bodies and protein.
- Early morning first void mid stream sample of urine (10 ml) collected to a sterile container is

recommended for urinary microalbumin testing. A random urine sample is an alternative.

- 24 hr urine specimens for protein should be collected to a bottle with no preservatives. It should be refrigerated during collection.

1.11.2 Protocol for the OGTT

Preparation of the patient:

Three days unrestricted, carbohydrate rich diet and activity.

No medication on the day of the test.

8 to 14 h fast.

For paediatric patients:

Children > 6 years: 8 -10 hr fast

Children < 6 years: before the next feed

No smoking is allowed during the test.

Patients should be seated and resting during the test.

Glucose load:

Adults - 75 g of anhydrous glucose or 82.5g of glucose monohydrate in 300 – 400 ml of water to be drunk over the course of 5 mts.

Children: 1.75 g/Kg up to 75 g of anhydrous glucose.

Timing of the test is from the beginning of the drink. Solutions containing glucose and oligosaccharides are commercially available and can be used as alternatives.

Plasma glucose sampling:

10 min before glucose load

120 min after glucose load

Factors affecting absorption and utilization of glucose should be recorded.(medications, infection, hospitalization, nausea and vomiting during the test)

If the patient complained of nausea following the glucose drink, a sample at 60 min should be collected.

Urine glucose can be additionally measured in case of hyperglycaemia

1.12 Notes on reporting (records of results):

Usage of SI units is preferred for all analytes.

It's recommended to record the results of all tests done in relation to screening, diagnosis and management of DM in an individual patient in a separate sheet of data attached to the patient's clinic records for quick reference and to facilitate testing for follow up at appropriate intervals.

1.13 References

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