

Guidelines for the management and care of diabetes mellitus

Quick reference guide

Diabetes mellitus is one of the most common noncommunicable diseases worldwide, and its epidemic proportion has placed it at the forefront of public health challenges. In the Eastern Mediterranean Region, there has been a rapid increase in the incidence of diabetes mellitus, mainly of type 2. It is now the fourth leading cause of death in the Region and an estimated 22 million people have diabetes out of a total adult population of 290 million. This quick reference guide aims to provide a readily accessible overview of the management and care of patients with diabetes mellitus.

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- Diabetes mellitus is a metabolic disorder of multiple etiology, characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.
- The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs.

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- The diagnosis of diabetes in an asymptomatic individual should never be made on the basis of a single abnormal glucose value. Verification of the diagnosis with repeat testing is required, unless an individual presents with unequivocal hyperglycaemia, along with its classic symptoms.
- The following table outlines the diagnostic values for diabetes mellitus and other categories of hyperglycaemia.

Diagnostic values for diabetes mellitus and other categories of hyperglycaemia

	Venous plasma glucose concentration	
	mmol/L	mg/dL
Diabetes mellitus		
fasting or	≥7.0	≥126
2-hour post-75 g glucose load	≥11.1	≥200
IGT		
fasting (if measured) and	<7.0	<126
2-hour post-75 g glucose load	≥7.8 and <11.1	≥140 and <200
IFG		
fasting and (if measured)	≥5.6 and <7.0	≥100 and <126
2-hour post-75 g glucose load	<7.8	<140

IGT: impaired glucose tolerance

IFG: impaired fasting glucose

- There are two main types of diabetes mellitus:
 - type 1, requiring insulin for survival
 - type 2, may or may not require insulin for metabolic control.
- Type 1 diabetes encompasses the majority of cases which are primarily due to pancreatic islet β -cell destruction and are prone to ketoacidosis.
- Type 2 includes the common major form of diabetes mellitus which results from defect(s) in insulin secretion, almost always with a major contribution from insulin resistance.
- Impaired glucose tolerance (IGT) refers to a condition intermediate between normoglycaemia and diabetes.
- A clinical stage of impaired fasting glycaemia (IFG) has been introduced to classify individuals who have fasting glucose values above the normal range, but below that diagnostic of diabetes.

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- Gestational diabetes is a state of carbohydrate intolerance resulting in hyperglycaemia of variable severity, with onset or first recognition during pregnancy. It does not exclude the possibility that the glucose intolerance may antedate pregnancy but has previously gone unrecognized. The definition applies irrespective of whether or not insulin is used for treatment or whether the condition persists after pregnancy.
- Other less common causes of diabetes mellitus are conditions in which the underlying defect or disease process can be identified; these can be caused by:
 - genetic defects in β -cells, such as maturity onset diabetes of the young
 - genetic defects in insulin action, such as Leprechaunism
 - diseases of the exocrine pancreas
 - endocrinopathies, such as Cushing syndrome, acromegaly and pheochromocytoma
 - drugs or chemicals, such as steroids and thiazides;
 - infections, such as rubella;
 - uncommon forms of immune-related diabetes, such as the type associated with insulin-receptor antibodies;
 - other rare genetic syndromes associated with diabetes, such as Klinefelter syndrome and Down syndrome.

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Oral glucose tolerance test

- This remains the definitive confirmatory diagnostic test for diabetes. Glucose levels ≥ 11.1 mmol/L (200 mg/dL) 2 hours after a 75 g oral glucose load are diagnostic of diabetes.

Fasting plasma glucose

- Fasting is defined as avoiding the consumption of any food or beverage, other than water, for at least 10–16 hours before testing. Fasting blood and plasma glucose levels are interpreted in the following table.

Interpretation of fasting blood and plasma glucose levels

Fasting plasma glucose	Interpretation
<5.6 mmol/L (<100 mg/dL)	Excludes diabetes (probably)
5.6–6.0 mmol/L (100–109 mg/dL)	Low probability, may be an indication for diagnostic testing among high risk individuals (OGTT)
6.1–6.9 mmol/L (110–125 mg/dL)	Indication for diagnostic testing (OGTT)
≥ 7.0 mmol/L (≥ 126 mg/dL)	Indicates diabetes, confirmation with repeat testing required

OGTT: oral glucose tolerance test

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- Given current knowledge, screening can be recommended only for research purposes related to the prevention of type 1 diabetes mellitus.

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- Among inhabitants of the Arabian Peninsula, the screening of asymptomatic adults for type 2 diabetes mellitus should be done for the following groups. If results are normal, screening should be repeated every three years. High risk characteristics include:
 - individuals aged ≥ 35 years
 - overweight (body mass index ≥ 25 kg/m²)
 - first-degree relative with type 2 diabetes
 - women with previous history of gestational diabetes mellitus or who delivered a baby weighing >4 kg
 - individuals diagnosed previously with IFG or IGT
 - hypertensive individual $>140/90$ mmHg
 - HDL cholesterol level ≤ 0.9 mmol/L (35 mg/dL) and/or triglyceride level >2.82 mmol/L (250 mg/dL)
 - other medical conditions associated with insulin resistance, e.g. polycystic ovary syndrome or acanthosis nigricans
 - history of vascular disease.

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- Screening for diabetes is justified on the grounds that early detection allows effective early intervention, thus diminishing the likelihood of the development of complications.
- Selective high-risk and opportunistic screening must be accompanied by confirmatory diagnosis and appropriate follow-up of new cases.
- Screening for IGT may be justified in high-risk populations but requires an OGTT for identification and a lifestyle intervention programme.
- Screening programmes should, therefore, be evaluated in terms of:
 - numbers of new cases detected
 - cost per new case detected
 - actions taken for individuals with positive test results
 - long-term benefits of early detection.
- People with screen-detected diabetes should be offered treatment and care.
- Diabetes is associated with a range of serious complications which result in reduced quality of life and premature mortality. Early detection and treatment is one strategy proposed for reducing diabetes health burden.

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- The objectives of therapy for diabetes are to:
 - eliminate symptoms of hyperglycaemia
 - achieve optimum control
 - reduce or eliminate microvascular and macrovascular complications of diabetes mellitus
 - treat associated disorders
 - allow the patient to achieve as normal a lifestyle as possible.
- The markers for diabetes control are blood glucose and glycated haemoglobin A1c (HbA1c). The recommended goals are shown in the following table.

Optimal control indicators for management of diabetes mellitus

Glycaemic control indicator	Normal	Target	Action needed
Plasma values			
Pre-meal glucose, mg/dL	<110	90–130	<90 or >150
mmol/L	<6.1	5.0–7.2	<5.0 or >8.3
Bedtime glucose, mg/dL	<120	110–150	<110 or >180
mmol/L	<6.7	6.1–8.3	<6.1 or >10.0
Whole blood values			
Pre-meal glucose, mg/dL	<100	80–120	<80 or >140
mmol/L	<5.5	4.4–6.7	<4.4 or >7.8
Bedtime glucose, mg/dL	<110	100–140	<100 or >160
mmol/L	<6.1	5.5–7.8	<5.5 or >8.9
HbA _{1c} (%)	<6.0	<7.0	>8.0

Self-monitoring of blood glucose (SMBG) should be available for all people diagnosed with diabetes, as an integral part of self-management education.

Each patient visit should cover the following items.

- Medical history, including:
 - symptoms of hyper- or hypoglycaemia
 - results of prior HbA_{1c} and home blood glucose records
 - meal patterns including frequency and content, and any change in weight
 - lifestyle and psychosocial elements
 - any acute complications such as infection, hypoglycaemia or ketoacidosis
 - any chronic complications related to vision, kidney, nerve, or the cardiovascular system
 - any associated cardiovascular risk factors such as a positive family history, hypertension, dyslipidaemia
 - review of all medications, ask if the patient is taking aspirin.
- Physical examination, including:
 - height and weight
 - vital signs, including blood pressure supine and sitting
 - fundoscopic examination, looking for any signs of retinopathy
 - oral examination, including gums
 - cardiovascular including evaluation for pulses and bruits
 - abdominal exam, assess liver size
 - foot examination, for oedema, ulcer and deformities
 - neurological examination: light, touch, vibration sense, reflexes, motor strength.
- Diagnostic studies, including:
 - fasting and 2-hour postprandial glucose, if feasible
 - quarterly HbA_{1c}
 - yearly chemistry panel, fasting lipid profile, urinalysis (including microscopy and urine microalbumin screening)
 - thyroid stimulating hormone for type 1 and for type 2, as indicated
 - ECG in adults at baseline, and then as clinically indicated.
- Treatment plan, formulated after discussion with the multidisciplinary diabetes team and the patient, including measures to:
 - control blood glucose
 - control and treat diabetic complications
 - address and treat associated risk factors such as obesity, physical inactivity, smoking, hypertension, and dyslipidaemia.
- Referral, if feasible, to:
 - diabetes educator, to evaluate patient's ability to perform self-monitoring of blood glucose and his/her ability to interpret the data
 - dietician
 - foot-care specialist
 - ophthalmologist for annual retinal screening, or more often as indicated
 - nephrologists, neurologist, and cardiologist, if needed.

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- The backbone of diabetes management is proper diet and regular exercise, which have to be individualized. Both could be the only management needed for controlling blood glucose in gestational diabetes and IGT and in type 2 diabetes in its early phase.
- Patients with type 2 diabetes may also require oral hypoglycaemic agents and/or insulin, while type 1 patients need insulin therapy to survive.
- The treatment plan for diabetes may include:
 - diabetes education: make structured patient education an integral part of the management
 - meal planning and nutritional recommendations: provide access to dietitian
 - exercise
 - anti-diabetic oral agents
 - insulin
 - management of associated conditions and complications.

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- Aspirin therapy (75–162 mg/day) is indicated as a secondary prevention in patients with evidence of cardiovascular disease.
- It is also indicated as primary prevention for cardiovascular disease in patients at risk, such as age >40, or with hypertension, smoking, obesity, and dyslipidaemia.

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- When lifestyle modification fail, therapeutic methods should be used that consist of the following options:
 - insulin sensitizers
 - insulin secretagogues
 - α -glucosidase inhibitors
 - insulin.

The following tables show the different groups and their doses. The physician's judgment will direct the method of treatment.

Types and mechanisms of action of oral anti-diabetic agents

Group	Name	Recommended daily dose	Mode of action
Insulin secretagogues			
sulfonylureas	glibenclamide	5–20 mg/day	Stimulate insulin secretion
	glyburide	2.5–20 mg/day	Stimulate insulin secretion
	glipizide	2.5–20 mg/day	Stimulate insulin secretion
	glimepiride	1–8 mg/day	Stimulate insulin secretion
	gliclazide	40–160 mg/day	Stimulate insulin secretion
	gliclazide LA	30 mg	Stimulate insulin secretion
benzoic acid derivative	repaglinide	3–16 mg/day	Stimulate insulin secretion
phenylalanine derivative	nateglinide	180–360 mg/day	Stimulate insulin secretion
Insulin sensitizers			
biguanide	metformin	0.5–2 gm/day	Decrease hepatic glucose production
			Increase insulin sensitivity
thiazolidinediones	rosiglitazone	2–8 mg/day	Increase insulin sensitivity
	pioglitazone	15–45 mg/day	Decrease hepatic glucose production
α -glucosidase inhibitors	acarbose	100–300 mg/day	Increase insulin sensitivity
	miglitol	100–300 mg/day	Decrease hepatic glucose production
			Delays carbohydrate absorption
			Delays carbohydrateabsorption

LA: long-acting

Types and modes of action of insulin

Insulin		Onset of action	Peak action	Duration of action
Insulin alone				
Short-acting	Regular/semilente	15–30 minutes	1–3 hours	5–7 hours
Intermediate-acting	NPH/lente	2–4 hours	8–10 hours	18–24 hours
Long-acting	ultralente	4–5 hours	8–14 hours	25–36 hours
Mixed insulin				
	Regular/NPH (%)			
	30/70			
	50/50			
	20/80	1–2 hours	2–12 hours	6–24 hours
Insulin analogs				
Fast-acting	lispro			
	aspart	5–15 min	1–1.5 hours	3–4 hours
Long-acting	glargine	1–2 hours	no peak	24 hours

NPH: neutral protamine Hagedorn

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- Hypoglycaemia in diabetic patients is an abnormally low concentration of glucose in the blood caused by insufficient food intake, excessive exercise, or overdosage with oral hypoglycaemic agents or insulin.
- For mild cases: taking small amounts of sugar or glucose-containing juice or food will usually help the person feel better within 10–15 minutes. Patients should carry rapidly absorbable carbohydrate with them at all times. Glucagon should be available in the home (and possibly in the school, day-care centre or workplace). In cases of severe hypoglycaemia and coma, the patient should be hospitalized.

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- Ketoacidosis mainly affects people with type 1 diabetes mellitus; it occurs when the body breaks down fatty acids and produces ketones.
- Major precipitating factors include infection, other acute illnesses, and omission of or insufficient insulin intake.
- With proper instruction on monitoring of blood glucose and urine ketones, insulin dose adjustment and maintenance of fluid intake many cases of diabetic ketoacidosis can be prevented.
- Hospitalization is needed.

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- Atherosclerosis is the most common complication of diabetes mellitus accounting for 75% of diabetes related-deaths. The occurrence of clinical events related to coronary artery disease is four times more common in diabetics.
- Risk factors are obesity, smoking, hypertension and hypercholesterolaemia.
- There is ample evidence that aspirin intake confers both primary and secondary prevention against cardiovascular disease in patients with diabetes.

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- Diabetic retinopathy is the leading cause of blindness and visual impairment in adults in the Eastern Mediterranean Region. Almost everyone with younger-onset type 1 diabetes mellitus will develop diabetic retinopathy after 20 years of the disease.
- Findings indicating the need for referral as soon as possible to an ophthalmologist for further management are:
 - non-proliferative retinopathy with macular involvement, or without macular involvement but with large circinate hard exudates
 - hard exudates within one disc diameter of the macula
 - pre-proliferative retinopathy.
- At present, no drugs are available to prevent development or progression of retinopathy.

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- Diabetic kidney disease is a major cause of premature death in diabetic patients, who are 17 times as prone to kidney disease as non-diabetics.
- It can be divided into several stages:
 - incipient (sub-clinical) nephropathy (albumin excretion rate of 20–200 µg/min or 30–300mg/24 hours).
 - clinical (or overt) nephropathy (albumin excretion rate >200 µg/min or >300 mg/24 hours)
 - advanced nephropathy with decrease in glomerular filtration rate
 - end-stage renal disease, necessitating dialysis or renal transplantation.
- Careful glucose and blood pressure control, and limitation of protein intake is essential in patients at risk.

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- Manifestations may occur in both the peripheral and autonomic nervous systems.
- Peripheral neuropathies include:
 - polyneuropathies, e.g. distal sensory-motor neuropathy and proximal motor neuropathy
 - focal neuropathies, e.g. mono-neuropathies (including cranial) and entrapment neuropathies.
 - multifocal neuropathies.
- Autonomic neuropathies may involve the following systems:
 - cardiovascular
 - gastrointestinal
 - genitourinary.
- The bare feet should be routinely examined. A simple screening procedure for distal sensory-motor neuropathy includes:
 - inspection of the feet
 - the grading of vibratory sensation at the dorsum of the toe
 - the grading of ankle reflexes.

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- Lifestyle changes aimed at weight control and increased physical activity are important objectives in the prevention of type 2 diabetes.
- Eastern Mediterranean countries should give priority to the development of community-based healthy lifestyle programmes that focus on:
 - maintaining a ‘healthy’ weight
 - an active lifestyle which includes regular physical activity
 - early identification of subjects at risk of developing type 2 diabetes mellitus
 - identifying subjects at high risk of noncommunicable diseases, such as hypertension, diabetes and heart disease
 - optimal maternal nutrition and weight maintenance
 - introduction of healthy lifestyle programmes in the early school years. These should focus on the prevention of risk factors, which will predispose to noncommunicable diseases in later life
 - cessation of smoking.
- The benefits of reducing body weight and increasing physical activity are not confined to diabetes – they also play a role in reducing heart disease and high blood pressure.

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- Secondary and tertiary prevention are key to reducing the risk of costly diabetic complications, as well as their associated disabilities.
- There is great potential for tertiary prevention with regard to blindness, limb amputation and adverse pregnancy outcomes.
- Rehabilitation and special assistance are required for those who do develop disabling complications.
- Overall, action taken early in the course of diabetes is more beneficial in terms of quality of life as well as being more cost-effective, especially if this action can prevent hospital admission.
- The United Kingdom Prospective Diabetes Study established the importance of good glucose control as well as good blood pressure control in prevention of vascular complications.

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For further information on diabetes mellitus, consult Khatib OMN (ed.) *Guidelines for the prevention, management and care of diabetes mellitus*, Cairo, World Health Organization Regional Office for the Eastern Mediterranean, 2006 (EMRO Technical Publications Series No. 32) on which this card is based, or contact:

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Design and layout by Ahmed Hassanein
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