

# **Guidelines for the management of hypertension in patients with diabetes mellitus**

## **Quick reference guide**

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 evidence-based facts regarding the management of hypertension patients with diabetes mellitus. They have been formulated to help improve the detection and management of hypertension in patients with diabetes mellitus, and hence decrease the associated microvascular and macrovascular complications.



## Rationale

- Macrovascular disease constitutes the major cause of diabetes mellitus mortality, with 80% of patients having and/or dying of cardiovascular, cerebrovascular or peripheral arterial disease. Patients with diabetes exhibit a two to four-fold increase in risk of coronary events compared to non-diabetic individuals.
- Although large-scale studies have shown a clear association between improvement in glycaemic control and reduction in microvascular end-organ damage (retinopathy, nephropathy and neuropathy), they have not been able to show a consistent similar relationship between glycaemic control and macrovascular complications.
- Many trials, however, have shown a benefit with respect to cardiovascular events, morbidity and mortality when coexistent hypertension is treated. In addition, control of hypertension is also beneficial to microvascular complications.
- This issue is of paramount importance since close to 60% of patients with diabetes are known to have hypertension. Therefore, aggressive strategies aimed at identifying and treating high blood pressure in patients with diabetes should lead to substantial reduction in the risk of cardiovascular morbidity and mortality.
- It is important to emphasize that hypertension is but one element of the metabolic syndrome in patients with type 2 diabetes mellitus. Due attention should be given to other coexisting cardiovascular risk factors – such as obesity and dyslipidaemia – and appropriate management of these conditions should be instituted.

## Definition and diagnosis of diabetes

### Definition

- 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.

### Diagnosis

- 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<br>mmol/L | mg/dL                 |
|----------------------------------|---|-----------------------|
| <b>Diabetes mellitus</b>         |   |                       |
| fasting <b>or</b>                | $\geq 7.0$                                    | $\geq 126$            |
| 2-hour post-75 g glucose load    | $\geq 11.1$                                   | $\geq 200$            |
| <b>IGT</b>                       |   |                       |
| fasting (if measured) <b>and</b> | $<7.0$  | $<126$                |
| 2-hour post-75 g glucose load    | $\geq 7.8$ and $<11.1$                        | $\geq 140$ and $<200$ |
| <b>IFG</b>                       |   |                       |
| fasting <b>and</b> (if measured) | $\geq 5.6$ and $<7.0$                         | $\geq 100$ and $<126$ |
| 2-hour post-75 g glucose load    | $<7.8$  | $<140$                |

IGT: impaired glucose tolerance

IFG: impaired fasting glucose

## Definition and diagnosis of hypertension

### Definition

- Hypertension is defined as a blood pressure  $\geq 140/90$  mmHg.
- Prehypertension refers to systolic blood pressure 120–139 mmHg or diastolic 80–89 mmHg.
- Normal blood pressure is referred to as  $<120/80$  mmHg.

### Classification of hypertension

| BP classification    | SBP (mmHg) | and | DBP (mmHg) |
|----------------------|------------|-----|------------|
| Normal               | $<120$     | and | $<80$      |
| Prehypertension      | 120–139    | or  | 80–89      |
| Stage 1 hypertension | 140–159    | or  | 90–99      |
| Stage 2 hypertension | $\geq 160$ | or  | $\geq 100$ |

SBP: systolic blood pressure

DBP: diastolic blood pressure

### Diagnosis

- Diagnosis should be made based on the mean of two or more blood pressure measurements, made while the patient is in the seated position.
- The possibility of secondary hypertension should be kept in mind and appropriate laboratory investigation undertaken as indicated.

## Risks associated with hypertension

- People with diabetes and hypertension have a two-fold increased risk of cardiovascular mortality compared to patients with diabetes alone. In addition, they have an increased risk of retinopathy and nephropathy.
- Lowering the blood pressure has been shown to have a beneficial effect on these complications. It has been shown that each 10 mmHg decrease in systolic blood pressure leads to a decrease in diabetes-related mortality by 15%, diabetes-related complications by 12% and myocardial infarctions by 11%.
- Multiple metabolic abnormalities associated with insulin resistance and increased cardiovascular risk such as dyslipidaemia, obesity and hypertension are already present at diagnosis. Consequently, treatment of hyperglycaemia alone cannot be expected to normalize the two to four-fold increased risk of cardiovascular mortality of these patients.
- In keeping with this, results of many intervention studies have demonstrated marked benefit from antihypertensive, lipid-lowering and antiplatelet therapy. Earlier recognition of at-risk individuals with screening and the subsequent investigation of a wide spectrum of preventive and corrective measures are recommended.

## Objectives of diabetes mellitus therapy

- The objectives of therapy for diabetes mellitus are:
  - to eliminate symptoms of hyperglycaemia
  - to achieve optimum control
  - to reduce or eliminate microvascular and macrovascular complications
  - to treat associated disorders
  - to allow the patient to achieve as normal a lifestyle as possible.
- The markers for diabetes control are blood glucose and HbA<sub>1c</sub>. The recommended goals are shown in the following table.

### Optimal control indicators for management of diabetes mellitus

| Glycaemic control indicator | Normal | Target  | Action needed |
|-----------------------------|--------|---------|---------------|
| <b>Plasma values</b>        |        |         |               |
| 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 |
| <b>Whole blood values</b>   |        |         |               |
| 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 <sub>1c</sub> (%)       | <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.

- The following table shows the recommendations for metabolic and non-metabolic targets (lipid profile, body mass index, blood pressure) for diabetic patients.

### Recommendations for metabolic and non-metabolic targets

|                                       | Good        | Borderline          | Poor        |
|---------------------------------------|-------------|---------------------|-------------|
| Total cholesterol, mg/dL (mmol/L)     | <200 (5.2)  | 200–250 (5.2–6.5)   | >250 (6.5)  |
| Fasting triglycerides, mg/dL (mmol/L) | <150 (1.7)  | 150–200 (1.7–2.2)   | >200 (2.2)  |
| HDL-cholesterol, mg/dL (mmol/L)       |             |                     |             |
| male                                  | >45 (1.15)  | 35–45 (0.9–1.15)    | <35 (0.9)   |
| female                                | >55 (1.40)  | 45–55 (1.15–1.40)   | <45 (1.15)  |
| LDL cholesterol mg/dL (mmol/L)        | <100 (2.56) | 100–130 (2.56–3.33) | >130 (3.33) |
| Total cholesterol/HDL ratio           |             |                     |             |
| male                                  | <6.4        |                     |             |
| female                                | <5.6        |                     |             |
| Body mass index (kg/m <sup>2</sup> )  |             |                     |             |
| male                                  | <25.0       | 25.0–27.0           | >27.0       |
| female                                | <24.0       | 24.0–26.0           | >26.0       |
| Blood pressure (mmHg)                 | <130/80     |                     |             |

LDL: low-density lipid

HDL: high-density lipid

### Blood pressure goal

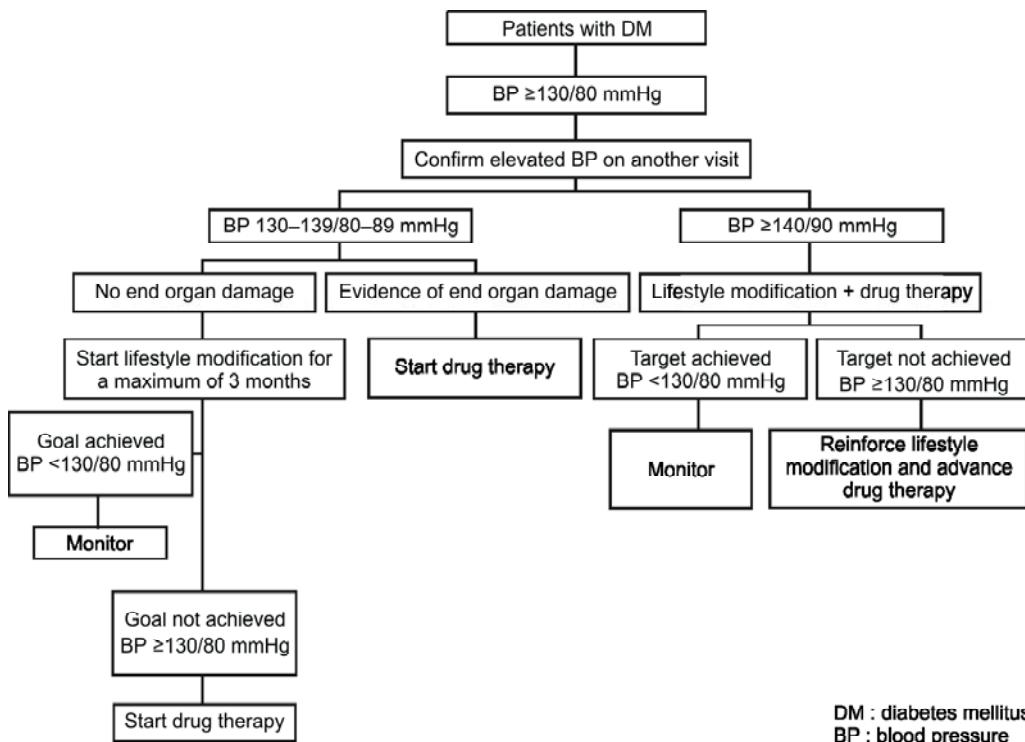
- There is no threshold for the risk of cardiovascular disease, but rather a continuous decrease in risk as blood pressure is reduced.
- The Hypertension Optimal Treatment (HOT) trial, the United Kingdom Prospective Diabetes Study (UKPDS) and the Appropriate Blood Pressure Control in Diabetes (ABCD) study showed a consistent benefit on cardiovascular events or mortality when blood pressure is reduced.
- Based on the above trials and on recommendations from international organizations, it is now accepted that the goal blood pressure level in diabetes mellitus should be <130/80 mmHg.

### Screening for hypertension

For screening purposes, the following guidelines are recommended.

- The patient's blood pressure should be checked at each clinic visit.
- Orthostatic measurements are indicated if autonomic neuropathy is suspected.
- If blood pressure is found to be ≥130/80 mmHg, it should be repeated on a separate visit.
- If the diagnosis is confirmed, treatment should be started.

## Treatment recommendations



*Suggested protocol for management of hypertension*

## Management

The following recommendations apply to the management of hypertension in patients with diabetes.

- Lifestyle modification (exercise, healthy diet, reducing weight and sodium intake) can lower blood pressure. Smoking cessation should be highly recommended.
- Thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and  $\beta$ -blockers are good initial therapy options in the treatment of uncomplicated hypertension (i.e. no evidence of nephropathy). They have been shown to lower cardiovascular events.
- Calcium channel blockers and  $\alpha$ -blockers can be used, but preferably as second-line therapy.
- Combination drug therapy is needed in a large number of patients in order to achieve target blood pressure.
- In patients with microalbuminuria in addition to hypertension, ACE inhibitors or ARBs are the drugs of choice because they have been shown to prevent or slow down the progression to macroalbuminuria.

- In patients with hypertension and congestive heart failure, ACE inhibitors are beneficial.
- $\beta$ -blockers are especially useful in patients with hypertension, post-myocardial infarction.
- In patients with nephropathy, careful follow-up of serum creatinine and potassium is recommended if diuretics, ACE inhibitors or ARBs are used.
- In the elderly, blood pressure should be lowered in a gradual fashion and over a longer period of time in order to avoid complications related to organ hypoperfusion.
- 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.

## Conclusion

- The following recommendations are made for the management of hypertension in patients with diabetes mellitus:
  - check blood pressure at each patient visit
  - target blood pressure level in all patients should be <130/80 mmHg
  - aggressively pursue management in order to achieve goals.
- Goal attainment should lead to a decrease in diabetes complications.
- The care of an individual with diabetes requires a multidisciplinary team. Central to the success of this team are the patient's participation, input, and enthusiasm. Members of the health team include primary care provider and/or diabetologists, nutritionist, and a diabetes educator.
- When the complications of diabetes mellitus arise, sub-specialists including neurologists, podiatrists, nephrologists, vascular surgeon, cardiologists and ophthalmologists are essential.
- Comprehensive diabetes mellitus care therefore means that optimal diabetes therapy involves more than plasma glucose management. It should also detect and manage diabetes mellitus complications and modify diabetes mellitus-related risk factors.
- The management of hypertension is only one of multiple strategies recommended by WHO for patients with diabetes. Further objectives of diabetes prevention and care include:
  - promotion of a healthy lifestyle
  - increasing community awareness about diabetes
  - primary diabetes prevention
  - development of national strategies for control of diabetes, obesity, hypertension and dyslipidaemia.

## Further reading

Chobanian AV, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. *Hypertension*, 2003, 42:1206-1252.

## Further information

For further information, consult Khatib OMN, El-Guindy MS (eds.) *Clinical guidelines for the management of hypertension*, Cairo, World Health Organization Regional Office for the Eastern Mediterranean, 2005 (EMRO Technical Publications Series No. 29) and 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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