Management of Type 2 Diabetes

INTRODUCTION

Diabetes mellitus (DM) is defined as a metabolic disorder of multiple etiologies, characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. It results from defects in insulin secretion, insulin action (resistance), or both. Developing guidelines for the management of DM should be given a priority in health care as the disease is a common, serious and costly health problem. According to the Ad Hoc Diabetes Reporting Group, Saudi Arabia is a high-prevalence country (12-23.7%). DM usually leads to many complications and, as a result, the economic burden of the disease is enormous. Good control is associated with reduced morbidity and mortality. Diabetic patients should be managed by a team rather than one physician. Lack of consistent care causes confusion in patients and reduces their compliance. Finally, the emotional cost on the patient and his family is huge, as the disease is commonly associated with anxiety, impotence, disturbed family life, and increased fatigue and irritability.

DIAGNOSIS

The criteria for the diagnosis of DM and impaired glucose tolerance have changed many times over the last decade. These changes were based on the epidemiological studies that looked at the association between different glucose levels and the incidence of complications. The most recent criteria are summarized in Figure 1.
MANAGEMENT
The management of patients with diabetes is classified in the current review under the following categories: a) Non-Pharmacological, b) Pharmacological, c) Monitoring of glycemic control, d) Prevention, e) Clinic organization and f) Referral and admission.

a. Non-Pharmacological

i. Psycho-Social Aspects.
The psycho-social impact of the disease should not be underestimated. Doctors should learn the communication skills as well as the skills of breaking bad news to patients when informing them of the diagnosis for the first time. These skills will no doubt enhance their ability to detect and treat psychological disorders associated with diabetes.

The patient may experience various degrees of anxiety and fear of complications, or may be affected socially as a result of the stigma or embarrassment leading to his/her isolation and low self-esteem.13

Social support from a family network or other sources, such as a diabetes support organization, and emotional well-being are crucial in achieving effective self-management of diabetes.14

Improvements in glycemic control are associated with the improvement in quality of life, provided there is no increase in hypoglycemic symptoms. Severe hypoglycemia may adversely affect the quality of life among patients treated with insulin, particularly newly diagnosed patients; multiple insulin injections were not found to adversely affect the quality of life.15

ii. Health Education
Diabetes education is the cornerstone of the care of diabetic patients who aspire to achieve successful health-related outcomes. In this respect, the role of the physician as “the coordinator”, is essential to ensure that the quality of diabetes education is delivered through a coordinated systematic approach. The instructional team should be composed of at least a trained nurse and a physician.

The following health education guidelines need to be considered13 (Appendix 1):
1. The patient must be taught self-care to be his (her) own doctor, dietician and laboratory technician (health promotion approach).
2. Suitably trained nurses and dieticians are possibly in a better position to deliver patient education than the physician; so they should be utilized properly for that purpose.
3. The education of the team members is of paramount importance and should precede the implementation of the protocol.

iii. Physical activity
Several long-term studies have demonstrated a consistent beneficial effect of regular physical activity on carbohydrate metabolism and insulin sensitivity, and their benefits can be maintained for at least 5 years. These studies employed physical activity regimens, three to four times a week, in 30-60-minute sessions. Improvements in HbA1c were generally 10-20% of baseline and were most marked in patients with Type 2 diabetes, particularly the most insulin resistant.16

A combination of physical activity and wise food choices can help to reach the target weight and maintain it.16 Patients should be informed that any type of exercise is useful, including walking to the mosque or the grocery, performing the house work and walking around the house.

iv. Diet
Many Type 2 diabetic patients are overweight and insulin resistant; therefore, medical nutrition therapy should concentrate on lifestyle changes that result in reduced energy intake along with exercise. Healthy lifestyle strategies help in the
control of blood sugar, dyslipidemia, and blood pressure. These strategies should therefore, be implemented at an early stage after the diagnosis of diabetes. It is recommended that a competent dietitian be included in the out-patient management of diabetic patients.

Studies on healthy subjects and those at risk of developing type 2 diabetes, support the importance of including foods containing carbohydrate, particularly from whole grains, fruits, vegetables, and low-fat milk in the diet of people with diabetes.17

In type 2 diabetic patients, there is a strong evidence that the ingestion of very large amounts of fibers are necessary to confer metabolic benefits on glycemic control, hyperinsulinemia, and plasma lipids.18

The component of the diet that has the greatest influence on blood glucose is carbohydrate. Other macronutrients in the diet such as fat and protein, can influence the postprandial blood glucose level, however. The total amount of carbohydrate consumed is a strong predictor of glycemic response, and, thus, monitoring total grams of carbohydrate, whether by use of exchanges or carbohydrate counting, remains a key strategy in achieving glycemic control.19 A recent meta-analysis found that the low glycemic index diet, as compared to high glycemic index diet had a significant effect on improving glycemic control.20
Protein intake should account for 15-20% of average energy intake. In individuals with microalbuminuria, reduction of protein to 0.8-1.0 g per kg body weight per day while in individuals with overt nephropathy, reduction to 0.8 g per kg body weight per day may slow the progression of nephropathy.\(^{18}\)

Nowadays, artificial sweeteners especially aspartame are added to a wide variety of drinks and drugs, and according to the current literature, the possible risk of cancer seems negligible and there is no convincing evidence that they are carcinogenic.\(^{21}\)

b. Pharmacological Management Guideline
A stepwise approach is recommended to lower and maintain HbA\(_{1c}\) to as close to physiological levels as possible (Figure 2).\(^{22}\) It was shown, beyond doubt, that a lower threshold for starting insulin in type 2 patients is associated with reduced long term complications.\(^{23}\) The early addition of insulin when maximum sulfonylurea therapy is inadequate, can significantly improve glycemic control without promoting increased hypoglycemia or weight gain.\(^{24}\) All therapies should be used in the context of continuing lifestyle intervention. Agreement to diet therapy should be discussed with people with diabetes and monitored when the level of glucose control is problematic. If the patient is not complying with diet or drugs, then his motivation towards following the recommended action should take precedence over increasing the drug dose. Insulin therapy is a necessary part of management for the majority of people with type 2 diabetes who survive the disease for 5 to 15 years.\(^{11}\) Therefore, it is important to prepare people with type 2 diabetes, well in advance, that insulin will almost certainly be required at some stage, due to the progressive nature of the disease. Insulin Glargine is a good choice for patients who suffer from frequent hypoglycemic attacks as it causes significantly less nocturnal hypoglycemia than NPH, thereby, reducing a leading barrier to initiating insulin.\(^{25}\) If fasting glucose is normal, while daytime glucose levels are above target levels, an intermediate-acting insulin, 6 to 10 units at breakfast time, should be added. Metformin should be continued when insulin is added. The combination therapy with Metformin and insulin improves glycemic control and reduces insulin requirements.\(^{26}\) The decision to start on conservative management (e.g. diet, exercise) or oral hypoglycemic drugs or insulin depends on many factors\(^{14}\) as shown in Figure 3.

c. Monitoring of Glycemic Control

i. Blood Glucose Targets
HbA\(_{1c}\) levels should be as close to physiological levels as possible, preferably less than 7%. Regular monitoring of HbA\(_{1c}\) results in improvement of metabolic control, and fewer hospitalizations prompted by poorly controlled glucose levels.\(^{27}\) Lower HbA\(_{1c}\) targets are particularly advisable for young people, in the first few years after diagnosis of diabetes, in the presence of complications of diabetes or multiple risk factors such as hypertension and hyperlipidemia\(^{1}\) and when the risk of hypoglycemia is minimal as in patients on insulin sensitizers (e.g. the Metformin or Glitazone) and those on alpha-glucosidase inhibitors such as Acarbose. Higher HbA\(_{1c}\) targets may be advisable for older people who are frail or have significant co-morbidities, for those with hypoglycemic unawareness and who suffer frequent hypoglycemic episodes as well as for those at risk of severe hypoglycemia (on insulin or insulin secretagogue) who live alone or have poor social supports.\(^{1}\)

ii. For which patients is self-monitoring of Blood Glucose (SMBG) advisable?
Type 1 and type 2 patients requiring insulin\(^{1,28}\) should be encouraged to check their blood sugar themselves and record the measurements on a chart.

d. Prevention
Prevention is an important issue in the management of diabetic patients. It should include
all the three levels of prevention: primary, secondary and tertiary.

I. Primary Prevention

i. Control of other Risk Factors

a. Obesity

In the past, type 2 diabetes affected primarily individuals older than 40 years of age. However, the increasing prevalence of childhood obesity has led to a marked increase in type 2 diabetes in adolescents and young adults.

A large number of epidemiological studies have shown that obesity and a sedentary lifestyle are independently related to the chances of developing diabetes. Data from the Nurses' Health Study suggest that the lowest risk of diabetes occurs in individuals who have a BMI <21, with increasing prevalence as the obesity levels increase.29

Similarly, several intervention studies have found that weight loss and increased physical activity help prevent or delay the development of type 2 diabetes among person with IGT.30, 31

b. Blood lipid (Table 1)

For patients with diabetes mellitus ‘Coronary Heart Disease (CHD) risk equivalent’, the overall goal is an LDL-C level [less than 2.6 mmol/l (<100 mg/dl)].32 Triglycerides (TGs) are also considered a risk factor of CHD.32,33 The target of TGs should be less than 1.7 mmol/l (150 mg/dl). If TGs are less than 5.7 mmol/l (500 mg/dl), it is recommended LDL-C to be lowered first; but if TGs are higher then TGs be lowered with the use of fibrates and nicotinic acid to prevent pancreatitis.32 Lipids should be measured annually or more frequently if not under control.

c. Blood pressure

The benefits of good blood pressure control in patients with diabetes exceed the benefits of tight glycemic control and extend not only to the prevention of macrovascular disease, but also to the prevention of microvascular complications.34,35

In one study, patients with diabetes who were randomized to a target diastolic blood pressure of 80 mmHg or less had a 50% reduction in major cardiovascular events compared with those with a target diastolic blood pressure of 90 or less.36 Two studies (The LIFE and the ALLHAT)37,38 have demonstrated that adequate BP control improves CVD outcomes, especially stroke, when aggressive BP targets are achieved. It is, therefore, recommended that blood pressure in diabetic patients should be controlled to levels of 130/80 mm Hg or lower.35

Both Angiotensin-converting enzyme (ACE) inhibitors and Angiotensin receptor blockers (ARB) are considered the first-line antihypertensive therapy for patients with both diabetes and hypertension; both agents have been shown to reduce long term complications.39,40

Most diabetic patients with hypertension require combination therapy to achieve optimal blood pressure goals. Thiazide-type diuretics are beneficial in diabetic patients, either alone or as part of a combined regimen.

Table 1: Optional risk factor levels for people with diabetes

| Lipid fraction         | Value          |
|------------------------|----------------|
| Total cholesterol      | <4 mmol/l      |
| LDL cholesterol        | <2.6 mmol/l    |
| HDL cholesterol        | >1 mmol/l      |
| TC:HDL ratio           | <4.5           |
| Triglycerides          | <1.7 mmol/l    |

| Blood pressure (BP)                              | Systolic BP | Diastolic BP |
|--------------------------------------------------|-------------|--------------|
| People with diabetes or cardiovascular disease   | <130 mm Hg  | <80 mm Hg    |
| People with diabetes and overt nephropathy,     |             |              |
| microalbuminuria or other renal disease          | Aggressive BP control is recommended, usually two BP-lowering agents including an ACE-inhibitor or A2 receptor-blocker, if tolerated, to prevent disease progression |

ii. Care of Patients with Impaired Glucose Tolerance (IGT)

There is growing evidence that at above normal glucose levels but below the diabetes diagnostic threshold, nowadays referred to as pre-diabetes, there is a substantially increased risk of cardiovascular disease (CVD) and death. In those individuals, CVD risk factors are also more prevalent.

When obese subjects with IGT received intensive individualized instruction on weight reduction, food intake, and guidance on increasing physical activity (intervention group), there was a 58% relative reduction in the incidence of diabetes after an average follow-up of 3.2 years.30 Furthermore, Metformin was shown to reduce the risk of diabetes by 31%.31 Similarly, Acarbose and Troglitazone reduced the risk of DM by 32% and 56%, respectively.41
iii. Aspirin Therapy
Meta-analyses of studies among diabetic patients support the view that low-dose aspirin therapy should be prescribed as a secondary prevention strategy, and as a primary prevention strategy (if no contraindications exist) in adults with diabetes who are at high risk of cardiovascular events. Furthermore, trials had demonstrated a significant benefit of aspirin versus no aspirin in reducing the composite end-point of cardiovascular deaths, stroke, or myocardial infarction among high-risk individuals, including those with diabetes.

iv. Smoking cessation
Studies of diabetic patients who smoked had found a heightened risk of morbidity, premature death, macrovascular and microvascular complications of DM as compared to non-smokers; smoking may have a role in the development of type 2 diabetes. Education of diabetic patients on the adverse effects of smoking is of paramount importance and counseling smokers to quit this habit was found to be cost-effective.

v. Vaccination
Patients with diabetes are at high risk for complications, hospitalization, and death from influenza and pneumococcal disease. The risk is greater among patients with end organ complications of cardiac and renal disease.

Vaccinating individuals at high risk before the influenza season each year is the most effective measure for reducing the negative impact of influenza on their health. Therefore, the influenza vaccine should be recommended for patients with diabetes, aged ≥6 months.

II. Secondary Prevention

Early diagnosis and screening
Checking fasting blood sugar is a relatively cheap and simple procedure. The incidence and prevalence of DM in Saudi Arabia increases significantly after the age of 30 years. Therefore, we recommend the screening for DM among asymptomatic Saudi patients aged 30 years and above. Screening is more important among obese individuals who have a first degree relative with diabetes, are hypertensive ≥140/90, have been diagnosed with gestational diabetes mellitus (GDM), have dyslipidaemia and those with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG).

III. Tertiary Prevention

Screening for complications
a. Diabetic Nephropathy
It is defined as increased urinary albumin excretion (UAE) in the absence of other renal diseases. Around 40% of type 2 diabetic patients suffer some sort of nephropathy, which increases the risk of death, mainly resulting from cardiovascular diseases.

Microalbuminuria is defined as albumin excretion rate (AER) of 30 to 300 mg/d, and overt proteinuria, as an AER greater than 300 mg/d. Urinary albumin to creatinine ratio (ACR), from first-morning voided samples, correlates well with 24-hour urinary albumin level. Therefore, it has been recommended for routine screening of patients with DM. Microalbuminuria is also defined as urinary ACR ≥ 2.5 mg/mmol (men) and ≥ 3.5 mg/mmol (women), while proteinuria is defined as urinary ACR ≥ 30 mg/mmol.

Screening for microalbuminuria should be requested for all Type 2 diabetes at the time of diagnosis and annually thereafter. Patients with albuminuria of any degree should undergo an evaluation for the presence of co-morbid associations, especially retinopathy and macrovascular disease.

The following strategies were found to be effective for the control of diabetic nephropathy: achieving the best metabolic control (HbA1c <7%), treating hypertension (<130/80 mmHg or <125/75 mmHg if proteinuria >1.0 g/24h and increased serum creatinine), using drugs like ACE-inhibitors or angiotensin II receptor blockers and treating dyslipidemia (LDL cholesterol <2.6 mmol/l).

b. Diabetic Neuropathy
About half of all people with diabetes suffer some degree of diabetic neuropathy which is usually present as either a polynuropathy or a mononeuropathy.

i. Peripheral neuropathy
Diabetic peripheral neuropathy may present with positive symptoms including pain, burning, and numbness, or negative symptoms, such as loss of sensation, as the disease progresses. The most common form of diabetic neuropathy is a polynuropathy characterized by the loss of peripheral sensation.
Neurological assessment of lower limbs should be performed for newly diagnosed diabetic patients and then annually or according to the presenting symptoms. In order to confirm the diagnosis, such patients are referred for nerve conduction studies.

Based on randomized controlled trials, the drug, gabapentin showed good efficacy, a favourable side-effect profile with lack of drug interactions and therefore it remains the first choice treatment in painful diabetic neuropathy, especially in the elderly.

ii. Autonomic neuropathy
Diabetic autonomic neuropathy (DAN) is a serious common complication. It is associated with an increased risk of cardiovascular mortality as well as multiple symptoms and impairments.

DAN may affect many body systems especially gastrointestinal [GI] and genitourinary tracts and the cardiovascular system. Constipation is the most common lower-GI symptom but may alternate with episodes of diarrhea.

In men, DAN may cause loss of penile erection and/or retrograde ejaculation. There is no curative therapy for DAN and usually symptomatic treatment is given.

c. Diabetic Retinopathy
Diabetic retinopathy (DR) and diabetic macular edema (DME) are common microvascular complications in patients with diabetes and may have a sudden and debilitating impact on visual acuity (VA), eventually leading to blindness.

Early detection of retinal abnormalities is essential in preventing DR/DME and loss of vision.

Ophthalmoscopy is a useful screening procedure, easy to perform and accessible to ophthalmologists and other physicians, and requires no specialized equipment. Compared with fundus photography, ophthalmoscopy by an experienced examiner was found to agree with grading by fundus photography in more than 85% of cases. In the hands of non-ophthalmologist, ophthalmoscopy was less sensitive than fundus photography in detecting both any DR and sight-threatening DR (sensitivity 63 vs. 79% and 66 vs. 87%, respectively).

The screening of all diabetic patients by an ophthalmologist should be undertaken annually or at short intervals based on retinal findings.

d. Coronary Heart Disease (CHD)
Diabetes is associated with a 2- to 4-fold increase in the risk of developing coronary artery disease. The risk of a myocardial infarction in patients with diabetes and no evidence of coronary artery disease, matches that of patients without diabetes who have had a previous myocardial infarction.

It was recommended that a noninvasive cardiac testing be performed for asymptomatic persons with diabetes who have peripheral arterial disease (PAD) or cerebrovascular disease, those with major or minor electrocardiographic (ECG) changes at rest, or those with ≥2 CVD risk factors. Various screening tests have been suggested and these include: thallium stress test, stress echocardiogram, or stress ECG.

The goals of early detection are not clearly defined in any of the currently available guidelines. In fact, there are few data on which to base recommendations for clinical practice for selecting the screening test for asymptomatic persons with diabetes.

There is convincing evidence, from population-based studies, that the ankle-brachial blood pressure index (ABI) is a useful noninvasive measure for the detection of subclinical PAD and that a low ABI may provide incremental information beyond that provided by cardiovascular risk factor measurements, "especially in people aged 50 years and older or those who appear to be at intermediate or higher risk for CVD, such as cigarette smokers or individuals with diabetes".

e. Diabetic foot
Foot ulcers are a significant complication of diabetes mellitus and often precede lower-extremity amputation. The most frequent underlying etiologies are neuropathy, trauma, deformity, high plantar pressures, and peripheral arterial disease.

All individuals with diabetes should receive an annual foot examination to identify high-risk foot conditions. The examination should include the assessment of protective sensation, foot structure, vascular status, and skin integrity. People at high-risk for diabetic foot should be evaluated more frequently and proper foot care strategies such as the use of footwear and debridement of callus offered. These strategies have been reported to decrease the incidence of lower extremity amputation by 49–85%.

Because foot ulcers are usually contaminated, culture of noninfected wounds is generally not
recommended. Polymicrobial infections predominate in severe diabetic foot infections and include a variety of aerobic gram-positive cocci, gram-negative rods, and anaerobes which necessitate aggressive intervention including proper antibiotic therapy with flucloxacinill, ciprofloxacin and metronidazole.

e. Clinic Organization
As a general guideline for a stable type 2 patient, three-monthly appointments are acceptable. The patient may visit earlier for repeat prescriptions or for other reasons. Newly-diagnosed patients usually need shorter appointment intervals. A check-list as a reminder for physicians should be developed to improve the care of diabetic patients (an example in appendix 2).

f. Threshold for referral and Admission
The indications for referral vary among physicians based on their competence and interest and between different sittings based on the availability of medications, other facilities and supporting staff such as diabetic educators, social workers, dieticians etc. Concerning the decision for admission, while nothing was discussed in many of the guidelines revised, we believe that the majority of physicians agree on certain clear indications such as in cases presenting with ketoacidosis, non-ketotic hyperosmolar coma, certain cases of diabetic foot and patients with severe infections or septicemia. Other reasons for admission could be uncontrolled diabetes mellitus due to social reasons and adjustment problems. While there is no clear threshold for admission, the following factors may have an influence on the doctor's decision to admit such as the presence of other acute illnesses (e.g. pneumonia) or chronic illnesses (e.g. Bronchial Asthma).

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Appendix 1: EDUCATION CHECKLIST

| Education Checklist | Date |
|---------------------|------|
| 1. Explanation of diabetes |      |
| 2. Diabetic care supplied |      |
| 3. Explanation of anti-diabetic drugs: |      |
| a) Equipment |      |
| b) Technique |      |
| c) Action |      |
| d) Storage |      |
| 4. Understanding and treatment of hypoglycemia. |      |
| 5. Diabetes complications. |      |
| 6. Understanding diet. |      |
| 7. IMPORTANCE OF NEVER OMITTING INSULIN in case of illness e.g. diarrhea, vomiting and stress. |      |
| 8. Urinalysis (The patients should have urine dipsticks at home). |      |
| 9. Care of feet. |      |
| 10. Risk of smoking. |      |
| 11. Check need for pre-conception counseling |      |
| 12. Exercise. |      |
| 13. Blood glucose measurement technique. Type 2 patients on insulin should be advised to buy a glucometer. |      |
| 14. Patients’ home monitoring chart. |      |
| 15. Special circumstances as applicable such as shift work, fasting Ramadan, performing Hajj, contraception, driving and travel…etc |      |

Appendix 2: DIABETES CARE FLOW SHEET

**Every Visit***

| Date |  |
|------|---|
| BP < 130/80 |  |
| Weight (BMI kg/m$^2$) |  |
| Smoking Cessation |  |
| Preconception Counseling |  |
| Daily admin, ASA |  |
| Diet and Exercise |  |
| Self management goals |  |
| Review BG record |  |

| Date |  |
|------|---|
| HbA$_{1c}$ < 7% |  |

**Quarterly**

| Date |  |
|------|---|
| Foot exam (comprehensive with monofilament) |  |
| LDL < 2.6 mmol/l |  |
| HDL > 1 mmol/l |  |
| Triglycerides < 1.7 mmol/l |  |
| Albumin/Creatinine ratio: <2.5 mg/mmol (men) or <3.5 mg/mmol (women) or Microalbuminuria <30 mg/d |  |
| Dilated eye exam (refer to ophthalmology) |  |
| Influenza Vaccine |  |
| Pneumococcal Vaccine |  |
| Diabetes Education |  |
| Psycho-social Screen |  |

**Annual/Periodic**

| Date |  |
|------|---|

*Every visit = diabetes focused visit which is recommended to be every 3-6 months and more often if needed.*