Lecture –[2] Fifth year Dr.Mahir Al-Talah

Endocrinology Diabetes mellitus

Investigations of Diabetes mellites

Urine testing

Glucose;

Testing the urine for glucose with dipsticks is a common screening procedure for detecting diabetes. If possible, testing should be performed on urine passed 1-2 hours after a meal to maximise sensitivity. The greatest disadvantage of urinary glucose measurement is the individual variation in ***renal threshold for glucose***. The most common cause of glycosuria is a low renal threshold, which is common during pregnancy and in young people; ***'renal glycosuria'*** is a benign condition unrelated to diabetes.

***Ketones*;**

Ketone bodies can be identified by the nitroprusside reaction, which measures acetoacetate, using either tablets or dipsticks.

Ketonuria may be found in normal people who have been fasting or exercising strenuously for long periods, who have been vomiting repeatedly, or who have been eating a diet high in fat and low in carbohydrate.

Ketonuria is therefore 'not pathognomonic' of diabetes but, if associated with glycosuria, the diagnosis of diabetes is highly likely.

***Protein*;**

Microalbuminuria or proteinuria, in the absence of urinary tract infection, is an important indicator of the development of ***diabetic nephropathy*** and/or ***increased risk of macrovascular disease.***

Blood testing

***Glucose*;**

Blood glucose can also be measured with colorimetric or other testing sticks, which are often read with a portable electronic meter. These are used for capillary (fingerprick) testing to monitor diabetes treatment. To make the diagnosis of diabetes, the blood glucose concentration should be estimated using an accurate laboratory method rather than a portable technique.

Glucose concentrations are lower in ***venous*** than ***in arterial or capillary*** (fingerprick) blood. Whole blood glucose concentrations are ***lower than plasma concentrations*** because red blood cells contain relatively little glucose. ***In general, venous plasma values are the most reliable for diagnostic purposes.***

Glycated haemoglobin;

Glycated hemoglobin provides an accurate and objective measure of glycemic control over a period of weeks to months (***past three months***).

Hemoglobin is one part of a red blood cell. It carries oxygen throughout the body. The glucose (sugar) in blood attaches to the hemoglobin, where it stays for the life of the red blood cell. The combined hemoglobin and glucose unit is called ***"Hemoglobin A1c (HbA1c)***". This test measures the percentage of the total hemoglobin that has glucose attached to it. Because red blood cells live for about three months, these tests reflect glucose levels for the previous 3 months. So it allows assessment of glycemic control by repeated measurements every few months in patients with known diabetes, But usually within the normal range in patients with impaired glucose tolerance.

The rate of formation of HbA1c is directly proportional to the ambient blood glucose concentration; ***a rise of 1% in HbA1c*** corresponds to an approximate ***average increase of 2 mmol/L (36 mg/dL) in blood glucose***. Although HbA1c concentration reflects the integrated blood glucose control over the lifespan of the erythrocyte (120 days), half of the erythrocytes are replaced in 60 days and HbA1c is most sensitive to changes in glycaemic control occurring in the month before measurement.
HbA1c estimates may be erroneously diminished in anaemia or during pregnancy, and may be difficult to interpret with some assay methods in patients who have uraemia or a haemoglobinopathy.

***The oral glucose tolerance test (OGTT)*;**
The OGTT is a provocation test to examine the efficiency of the body to metabolise glucose. The OGTT provides information on latent diabetes states. The OGTT distinguishes metabolically healthy individuals from people with impaired glucose tolerance and those with diabetes.
The OGTT is more sensitive than FPG for the diagnosis of diabetes.
The OGTT is not used for the monitoring of day to day blood glucose control, which is done by HbA1c-, and repeated glucose measurement.
The OGTT is used mainly for diagnosis of IGT and in epidemiological population studies, but is not recommended or necessary for routine diagnostic use.

Indications for oral glucose tolerance test

Fasting plasma glucose 6.1-7.0 mmol/L (110-126 mg/dL)
Random plasma glucose 7.8-11.0 mmol/L (140-198 mg/dL)

"How to perform an oral glucose tolerance test (OGTT)"

Preparation before the test

Unrestricted carbohydrate diet for 3 days
Fasted overnight for at least 8 hrs
Rest for 30 mins
Remain seated for the duration of the test, with no smoking

"S*ampling"*

Plasma glucose is measured before and 2 hrs after a 75 g oral glucose drink

"Interpretation"

	Fasting plasma glucose		***120 min glucose***
IFG	6.1-6.9 mmol/L (110-125 g/L)		< 7.8 mmol/L (< 140 mg/dL)
IGT	<7.0 mmol/L (<126 g/L)	and	7.8-11.0 mmol/L (140-199 g/L)
Diabetes	≥ 7.0 mmol/L (≥126 g/L)	or	≥11.1 mmol/L (≥200 g/L)

Management of Diabetes mellitus.

GOALS

The goals of management can be divided into three stages:

(1) short term, involving immediate treatment to relieve symptoms such as polydipsia, polyuria, or acute infections;

(2) intermediate term, to return the patient to a physiologic state and social life that are as normal as possible; and

(3) long term, to prevent the development, or delay the progression, of the complications of diabetes.

The cornerstones of a comprehensive diabetes management plan ***include patient education, healthy nutrition,weight control, physical activity, self-monitoring of blood glucose (SMBG), and antihyperglycemic agents when necessary.***

Patient education aims to empower patients by equipping them with the necessary knowledge about diabetes and self-management skills with which to make meaningful decisions about their health on a daily basis.

BLOOD GLUCOSE MONITORING

SMBG with blood glucose meters, by all patients, facilitates adjustments in treatment and also acts as an educational tool for the patient. Ideally, SMBG should be performed as frequently as practicable—fasting, pre-prandial,

2 hours postprandial (especially in GDM; measure at 1 hour postprandial), at bedtime, and occasionally at 2:00 am to 3:00 am—and values should be recorded.

The HbA1c value (nonenzymatic irreversible glycosylation of the hemoglobin molecule, HbA1c, depends on ambient plasma glucose levels; the average life span of a red blood cell, and hence its HbA1c, is 120 days), by providing a measure of the average blood glucose level over the preceding 2 to 3 months, serves as an indicator of diabetes control. Testing frequency is 2 or more times per year in patients with T2DM with stable glycemic control and meeting treatment goals, and 4or more times per year for patients with T1DM, those with poor glycemic control, or those after therapy change.

Caution must be exercised in using HbA1c as the only gauge of diabetes control. Patients with wide fluctuations in blood glucose levels may sometimes have normal, average blood glucose levels and HbA1c. Elevated HbA1c despite normal FPG (good control) is frequently the result of elevated PPG (>200 mg/dL in 75% of patients with T2DM with HbA1c values ≥7%; HbA1c = FPG + PPG).Records of SMBG are usually more informative and useful for making therapeutic decisions than HbA1c. The HbA1c in measuring the average blood glucose level over the preceding 2 to 3 months may be close to goal while actual daily blood glucose levels fluctuate between hyperglycemia and hypoglycemia.

The importance of PPG cannot be overestimated. Elevated PPG, not FPG, is an independent risk factor for cardiovascular disease and all-cause mortality.

Spuriously low levels of HbA1c may be seen in patients with hemoglobinopathies such as homozygous or heterozygous HbS, C, G, or H. Variable levels of HbA1c may be noted with HbE or persistent HbF.

β-thalassemia and sickle cell trait, with increased frequency of hemolysis, result in shortened red blood cell life span, reduced time available for glycosylation of hemoglobin, and thus falsely low HbA1c levels.
Measurement of serum fructosamine may be a useful marker for shorter-term assessment of integrated glucose concentrations (2 to 4 weeks), for example, during pregnancy.

Treatment Goals for Adults with Diabetes

Glycemic control	
HbA1c	<7.0%c
Preprandial capillary plasma glucose	4.4-7.2 mmol/L (80-130 mg/dL)
Peak postprandial capillary plasma glucose	<10.0 mmol/L (<180 mg/dL)
Blood pressure	<140/90 mmHge
Lipids	
Low-density lipoprotein	<2.6 mmol/L (100 mg/dL)
High-density lipoprotein	>1 mmol/L (40 mg/dL) in men >1.3 mmol/L (50 mg/dL) in women
Triglycerides	<1.7 mmol/L (150 mg/dL)

STANDARDS OF CARE AND SPECIFIC TREATMENT GOALS

Regular patient assessment includes weight, blood pressure, pulse, SMBG records, foot examination, and discussionabout smoking cessation at every office visit, with quarterly assessment of HbA1c.
Determination of microalbuminuria, serum creatinine levels, dilated retinal examination, general physical, neurologic (with autonomic testing), cardiac, nephrology, and dental examinations, with comprehensive foot evaluation, should be performed yearly, provided all are normal. Influenza vaccine should be administered yearly and Pneumovax every 5 years. Following the initial measurement of serum lipids, the frequency of reevaluation is dictated by results and treatment and should be done at least yearly.
Aspirin therapy should be considered in every patient with diabetes, provided that no contraindications exist.
Goals for lipid levels are influenced by cardiovascular risk factors. Optimal values are LDL cholesterol under 100 mg/dL (2.6 mmol/L) or less than 70 mg/dL in patients with established cardiovascular disease, HDL cholesterol over 45 mg/dL (1.15 mmol/L) for men and over 55 mg/dL (1.4 mmol/L) for women, and triglycerides under 150 mg/dL (1.7 mmol/L).
Hydroxymethylglutaryl coenzyme A reductase inhibitors, or statins, are highly effective in the management of diabetic dyslipidemia and, together with their anti-inflammatory actions and improvement in endothelial function, may reduce the risk for cardiovascular events by about 30%. Fibrates or niacin (used with caution in patients with T2DM) may be required for lowering triglycerides or elevating HDL, respectively.
Combined use of several classes of agents may be necessary for lipid control. Combination tablets of ezetimibe and simvastatin fibrates with statins, and niacin with statins facilitate compliance and efficacy at lower doses than if usedseparately.

Normal urinary albumin-to-creatinine ratio is less than 30 mcg/mg.
Microalbuminuria refers to an albumin-to-creatinine ratio of 30 to 299 mcg/mg and macroalbuminuria greater than 300 mcg/mg.

MEDICAL NUTRITION THERAPY

Daily energy requirements include consumption of a balanced, healthy diet composed of 10% to 20% protein (1 g/kg body weight, provided no nephropathy exists), less than 35% total fat (10% saturated, ≤10% polyunsaturated, 10% to 20% monounsaturated and transunsaturated, and 200 to 300 mg cholesterol), and 45% to 60% carbohydrate.
Soluble fiber (15 g/1000 kcal) in the diet delays carbohydrate absorption (dampening the PPG peak) and improves serum lipid profiles. Insoluble fiber contributes to satiety (especially important if overweight) and gastrointestinal homeostasis.
Salt (NaCl) intake should be restricted to less than 6 g per day. Partial substitution of potassium chloride or magnesium chloride may be beneficial.

WEIGHT-MANAGEMENT THERAPY

Overweight (body mass index [BMI] of 25.0 to 29.9) and obesity (BMI 30) are major risk factors for T2DM and cardiovascular disease. (BMI = weight [kg]/height [m2]). As little as 5% to 10% weight loss in overweight and obese patients reduces the risk for diabetes and leads to increased insulin sensitivity, with improvement in glycemic control, and the possibility of a reduction or cessation of antihyperglycemic therapy.
This degree of weight loss also leads to significant improvements in dyslipidemia and blood pressure, as well as an increase in longevity.

EXERCISE THERAPY

As with nutrition and weight management, physical activity is recognized as a specific therapy for patients with diabetes and is an independent risk factor for death.
Benefits, many independent of associated weight loss, include improvements in the sense of well-being, blood pressure, endothelial function, insulin sensitivity, lipid profile (consistent reduction in very-low-density lipoprotein [VLDL]), cardiorespiratory fitness, and glycemic control, with reduction in HbA1c.
Notably, exercise itself, unless extreme, will not contribute to significant weight loss, but will, however, help in weight maintenance and prevention of weight gain. Ideally, this regimen involves moderate aerobic exercise (e.g., walking) for 60 to 90 minutes per day or vigorous exercise for 35minutes per day.
Blood glucose levels should be measured before any exercise activity is initiated. Exercise should not be undertaken in patients with FPG greater than 250 mg/dL (13.8 mmol/L) with ketones, or greater than 300 mg/dL (16.6 mmol/L) without ketones, because this may paradoxically precipitate DKA.
If FPG is less than 100 mg/dL (5.5 mmol/L), exercise may result in hypoglycemia, and carbohydrate should be consumed in advance. With the initiation of an exercise program, SMBG should be performed every 30 minutes during exercise lasting longer than 30 to 45 minutes; glucose or carbohydrate may need to be consumed, depending on glucose levels.