SYNOPSIS OF DIABETES MELLITUS

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INTRODUCTION

Diabetes mellitus is a metabolic disorder that is presently troubling the world, posing a great socio-economic burden to very nation. An overview on the definition, diagnosis, potential dangers and current prevention and treatment options available in putting a check to this disease will go a long way in helping physicians, diabetic patients and even diabetic relatives (whom themselves have an increased risk of developing the disease) in controlling the alarming increase in the prevalence of diabetes mellitus being experienced today.

DEFINITION

The term diabetes mellitus describes a chronic metabolic disorder of multiple aetiology characterized by hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from a relative or an absolute lack in insulin.

EPIDEMIOLOGY

Dramatically, over the past two decades the worldwide prevalence of DM has risen from an estimated 30 million cases in 1985 to 177 million in 2000. Based on current trends, over 360 million individuals will have diabetes by the year 2030. The prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly because of increasing obesity and reduced activity levels as countries become more industrialized.

With respect to sex distribution, the prevalence is similar in men and women throughout most age ranges (10.5% and 8.8% in individuals >20 years respectively) but is slightly greater in men >60 years.

Worldwide estimates project that in 2030 the greatest number of individuals with diabetes will be 45–64 years of age.

There exist a considerable geographic variation in the incidence of DM and this variability is likely due to genetic, behavioral, and environmental factors. Scandinavian countries have the highest incidence of type 1 DM (e.g., in Finland, the incidence is 35/100,000 per year) while the Pacific Rim has a much lower rate (in Japan and China, the incidence is 1–3/100,000 per year) of type 1 DM; Northern Europe and the United States have an intermediate rate (8–17/100,000 per year). In 2005, the CDC estimated that the prevalence of DM in the United States (age > 20 years) was; African Americans-13.3%, Latinos-9.5%, Native Americans (American Indians and Alaska natives) -15.1%, and non-Hispanic whites-8.7%.

Both males and females are affected.

Sex, age and ethnic background are important factors in determining risk of developing type 2 DM.

AETIOLOGY / RISK FACTORS

The causes/ risk factors for diabetes mellitus depend on the aetiological classification being looked at.

AETIOLOGICAL CLASSIFICATION OF DISORDERS OF GLYCAEMIA*

--Type 1 (beta-cell destruction, usually leading to absolute insulin deficiency)

A) Autoimmune

B) Idiopathic

--Type 2 (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance)

--Other specific types

Genetic defects of beta-cell function

Genetic defects in insulin action

Diseases of the exocrine pancreas

Endocrinopathies

Drug- or chemical-induced

Infections

Uncommon forms of immune-mediated diabetes

Other genetic syndromes sometimes associated with

Diabetes

--Gestational diabetes**

***As additional subtypes are discovered it is anticipated that they will be reclassified within their own specific category.**

****Includes the former categories of gestational impaired glucose tolerance and gestational diabetes.**

CULLED FROM: Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications Report of a WHO Consultation Part 1: Diagnosis and Classification of Diabetes Mellitus World Health Organization Department of Non-communicable Disease Surveillance Geneva.

CLINICAL FEATURES

This is a clinical condition that is described as a state of starvation in the midst of plenty. Some others describe it as a disease of plenty;

- Plenty urine
- Plenty sugar
- Plenty drinking
- Plenty eating
- Plenty problems (multiple complications)

The things that are not plenty in these conditions are:

- Insulin in type 1 patients (hyperinsulinaemia may occur in Type 2)
- Weight loss especially in type 1 (in type 2, depending on the level of control)
- Money for investigations and treatment (poverty).

TYPE 1 DIABETES MELLITUS

Although typically diagnosed in patients before age 30, it can present at any age due to variability in the rate of beta-cell destruction.

TYPE 2 DIABETES MELLITUS

Type 2 DM is known to account for 90-95% of cases of DM globally. In Africa, DM currently affects about 10 million people in the 20-79 year age group with the figure estimated to increase to 18 million by the year 2025. The prevalence of DM in this same age group is estimated to rise from 3.5% to 4.5%. A study by Nyenwe et al in Port- Harcourt, Nigeria in 2003 reported a crude prevalence rate of 6.8% for type 2 DM and a standardized prevalence rate of 7.9%. The National standardized prevalence rate of DM in Nigeria is 2.2% and the crude prevalence rate is 7.4% in individuals aged 45 years and above living in urban areas.

DIABETES IN PREGNANCY

Gestational diabetes is carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. This does not in any way exclude the

possibility that the glucose intolerance may antedate pregnancy but has been previously unrecognized. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy.

The risk factors for gestational diabetes mellitus are Obesity, Ethnicity (South Asian, black, Hispanic, Native American), Family history of type 2 diabetes, previous glucose abnormalities in pregnancy and previous macrosomia.

It is important to note that women who become pregnant and who are known to have diabetes mellitus which antedates pregnancy do not have gestational diabetes but have "diabetes mellitus and pregnancy" and should be treated accordingly before, during, and after the pregnancy.

In making a diagnosis of gestational diabetes mellitus a standard OGTT should be performed after overnight fasting (8–14 hours) by giving 75 g anhydrous glucose in 250–300 ml water. Plasma glucose is measured fasting and after 2 hours. Pregnant women who meet WHO criteria for diabetes mellitus or IGT are classified as having Gestational Diabetes Mellitus. After the pregnancy ends, the woman should be re–classified as having either diabetes mellitus, or IGT, or normal glucose tolerance based on the results of a 75 g OGTT six weeks or more after delivery. It is important to note that such women, regardless of the 6–week post–pregnancy result, are at increased risk of subsequently developing diabetes.

OTHER SPECIFIC TYPES

Other etiologies for diabetes mellitus include specific genetic defects in insulin secretion or action, metabolic abnormalities that impair insulin secretion, mitochondrial abnormalities, and a host of conditions that impair glucose tolerance. Mutations in the insulin receptor cause a group of rare disorders characterized by severe insulin resistance.

Maturity onset diabetes of the young (MODY) is a subtype of DM characterized by autosomal dominant inheritance, early onset of hyperglycemia (usually <25 years), and impairment in insulin secretion.

Also, diabetes can result from pancreatic exocrine disease when the majority of pancreatic islets are destroyed. Hormones that antagonize insulin action can also lead to diabetes mellitus. Thus, DM is often a feature of endocrinopathies such as acromegaly and Cushing's disease. Viral infections have been implicated in pancreatic islet destruction but are an extremely rare cause of DM.

Malnutrition-related DM

This condition also known as tropical diabetes tends to occur in malnourished children. It is commoner in the tropics where malnutrition and cassava consumption have been implicated as its aetiology. Individuals with this type of diabetes tend to have insulin resistance and often require high doses of insulin for control. It is associated with pancreatic fibrosis and calcification (fibrocalculous pancreatopathy). Patients with this type of DM may give a history of passing poorly digested food particles in their stools. They may also give a history of severe abdominal pain in the past.

It is important to note that a form of acute onset of type 1 diabetes mellitus, termed *fulminant diabetes*, has been noted in Japan and may be related to viral infection of islets.

INVESTIGATIONS

MAKING A DIAGNOSIS

FBS-- ≥ 126mg/dL or 7mmol/L

RBS-- ≥ 200mg/dL or 11.1mmol/L

OGTT*-- ≥ 126mg/dL and 2 hours postprandial of ≥ 210mg/dL
*The oral glucose tolerance test (OGTT) is principally used for diagnosis when blood glucose levels are equivocal, during pregnancy, or in epidemiological studies.

OTHER INVESTIGATIONS
FASTING SERUM LIPID PROFILE- may have hyperlipidaemia or dyslipidaemia
AUTOANTIBODY TESTING- type 1 DM individuals may have antibodies to islet cells, glutamic acid decarboxylase (GAD) and even insulin

LIVER FUNCTION TEST + SERUM PROTEINS – fatty liver can occur in diabetics and this may progress to chronic hepatitis with abnormal liver functions. Diabetes can be associated with liver conditions in disease states like; haemochromatosis, autoimmune hepatitis and hepatitis C viral infection. In such conditions patients with diabetes may come down with jaundice and other stigmata of liver disease. Those with autoimmune type 1 DM may have other autoimmune conditions like autoimmune haemolytic anaemia with jaundice as a feature.

INSULIN RESISTANCE – using the insulin clamp method or homeostasis model assessment method (HOMA) NB- a finding of acanthosis nigricans is suggestive of insulin resistance. It may also be a skin manifestation of an internal malignancy. It can be found around the neck, axillar, groin or anal region.

ECG- may show evidence of ischaemic heart disease. It is important to remember that they can suffer a silent myocardial infarction (painless MI)

CHEST X-RAY – may show cardiomegaly, hypertensive heart changes for those that are hypertensive and may show evidence of chest infection as they are prone to having infections. Lazy leukocyte/defective opsonization being responsible for the increased risk of infection. The hyperglycaemia is also known to the encourage growth of microbes.

URINALYSIS- may show protein, glucose and/ or ketones in urine depending on how the patient presents.

URINE M/C/S- may show evidence of infection

WOUND SWAB FOR M/C/S – may also show evidence of infection
DOPPLER SCAN- may be indicated in those with peripheral vascular disease.

COMPLICATIONS
Can be grouped into the ACUTE and the CHRONIC complications.

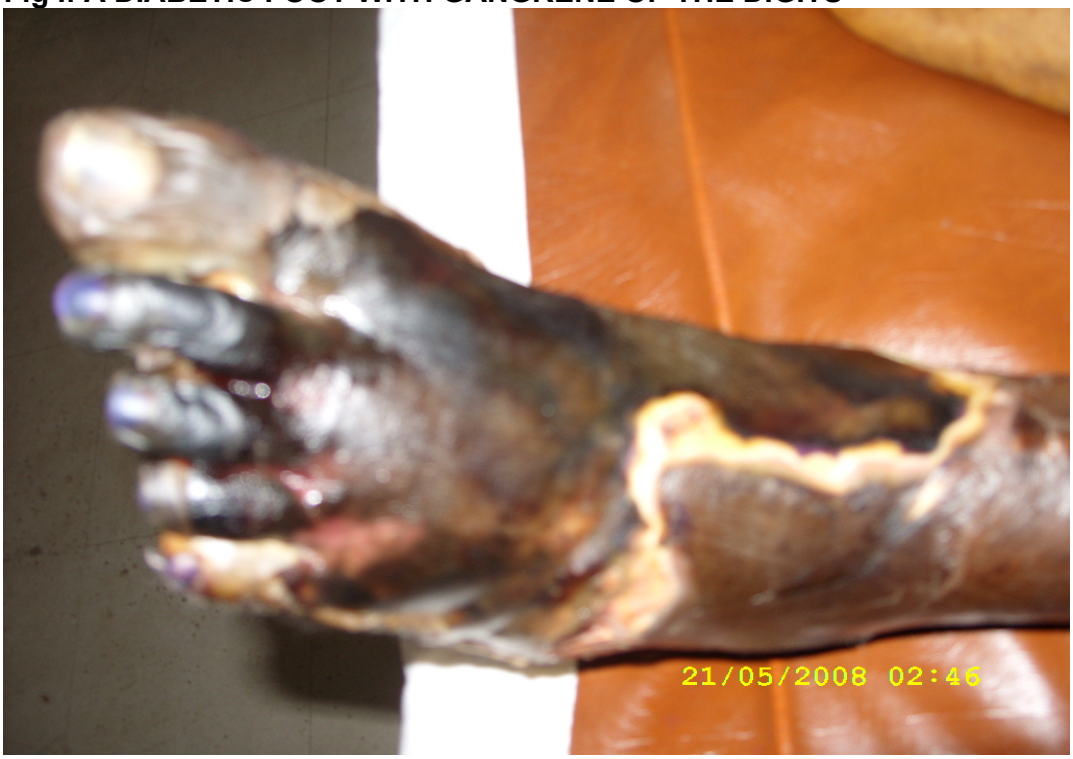
ACUTE COMPLICATIONS
Diabetic ketoacidosis
Hyperosmolar hyperglycaemic state (formerly honk)
Hypoglycaemia
Lactic acidosis
Acute circulatory failure

CHRONIC COMPLICATIONS
a) **Microvascular complications**
I. Diabetic retinopathy
II. Diabetic nephropathy
III. Peripheral neuropathy
b) **Macrovascular complications**
I. Peripheral vascular disease
II. Ischaemic heart disease
III. Stroke
c) **Others**
I. Fetal macrosomia
II. Intrauterine growth resriction
III. Intrauterine fetal death
IV. Cataracts
V. Diabetic dermopathy

VI. Bullae formation
VII. Foot ulcers
VIII. Recurrent boils
IX. Generalised pruritus
X. Gas gangrene
XI. Dupuytren's contracture

These are just some of the complications that can occur in diabetics.

Fig I: A DIABETIC FOOT WITH GANGRENE OF THE DIGITS



TREATMENTS
A) DRUGS
1. INSULIN

TYPE	APPEARANCE	ADDED PROTEIN	ZINC CONTENT (mg/100units)	DURATION (HOURS)
RAPID/SHORT				
Regular	Clear	None	0.01-0.04	5-8
Lispro	Clear	None	0.02	2-5
Aspart	Clear	None	0.0196	3-5
Glulisine	Clear	None	None	1-2.5
INTERMEDIATE				
NPH*	Cloudy	Protamine	0.016-0.04	18-24
Lente	Cloudy	None	0.2-0.25	18-24
SLOW (LONG)				
Ultralente	Cloudy	None	0.2-0.25	20-36
Protamine zinc	Cloudy	Protamine	0.2-0.25	24-36
Glargine				
Detemir	Clear	None	0.03	18-24
	Clear	None	0.065	6-24

INDICATIONS FOR INSULIN THERAPY

- TYPE 1 Diabetes mellitus
- Gestational Diabetes mellitus/ Diabetes in pregnancy
- Oral glucose lowering agents failure
- Treatment of Diabetic emergencies like DKA and HHS
- For patients going for surgery and even in post –op state
- Myocardial infarction/stroke/ diabetic foot ulcer
- Insulin can also be used in treating hyperkalaemia.

COMPLICATIONS OF INSULIN THERAPY

- Hypoglycaemia
- Weight gain
- Lipodystrophy/Lipohypertrophy
- Infections at injection sites
- Thrombophlebitis
- Insulin oedema
- Hypokalaemia

2. ORAL MEDICATIONS (SEE TABLE II)

Drug	Mechanism of Action	Examples	Agent-Specific Advantages	Agent-Specific Disadvantages	Contraindications/ Relative Contraindications
Biguanides	Hepatic glucose production, weight loss, glucose, utilization, insulin resistance	Metformin	Weight loss	Lactic acidosis, diarrhea, nausea	Serum creatinine >1.5 mg/dL (men) >1.4 mg/dL (women), CHF, radiographic contrast studies, seriously ill patients, acidosis
Alpha – Glucosidase inhibitors	Glucose absorption	Acarbose, Miglitol	Reduce postprandial glycemia	GI flatulence, liver function tests	Renal/liver disease
Dipeptidyl peptidase IV inhibitors	Prolong endogenous GLP-1 action	Sitagliptin	Does not cause hypoglycaemia		Reduce dose with renal disease
Insulin secretagogues—sulfonylureas	Insulin secretion	Chlorpropamide Tolazamide Tolbutamide Glimepiride Glipizide Glyburide	Lower fasting blood glucose	Hypoglycemia, weight gain	Renal/liver disease
Insulin secretagogues—nonsulfonylureas	Insulin secretion	Repaglinide Nateglinide	Short onset of action, lowers postprandial glucose	Hypoglycemia	Renal/liver disease
Thiazolidinediones	Insulin resistance, glucose utilization	Rosiglitazone, Pioglitazone	Lower insulin requirements	Peripheral edema, CHF, weight gain, fractures, macular edema; rosiglitazone may increase risk of MI	Congestive heart failure, liver disease

B. SURGERY – may be indicated in patients with Diabetic foot with gangrene. Islet cell transplantation alongside renal transplantation has been done in those with DM nephropathy.

C. NON DRUG TREATMENT
Diet, weight reduction and exercise

D. EXPERIMENTAL OPTIONS

CONCLUSION
Diabetes mellitus is a chronic clinical condition requiring a multidisciplinary care. Presently, it is a condition demanding an urgent action plan to curb its alarming prevalence. It is cost effective to prevent than to treat this disorder.

FURTHER READING

1. WHO Consultation Group. Definition, diagnosis and classification of diabetes mellitus and its complications; 2nd ed. Part 1: Diagnosis and classification of diabetes mellitus WHO/NCD/NCS/99, Geneva, World Health Organization, 1999; 1-59.

2. Nyenwe EA, Odia OJ, Ihekwaba AE, Ojule A, Babatunde S. Type 2 Diabetes in Adult Nigerians: Study of its prevalence and risk factors in Port-Harcourt, Nigeria. Diabetes Res Clin Pract 2003; 62:177-185.

3. Akinkugbe OO, Akinyanju OO. (Editors) Non-communicable Disease in Nigeria.Final report of National Survey, Federal Ministry of Health and Social Services, Lagos 1997.

4. Fauci AS, Braunwald E, Kasper DL et al. Harrison's Principles of Internal Medicine, 17th Edition,2008, The McGraw-Hill , United States of America.

5. Kronenberg HM, Melmed S, Polonosky KS et al. Williams Textbook of Endocrinology, 11th ed. Philadelphia, PA: Saunders Elsevier, 2008.

6. Zollo AJ. Medical Secrets, 4th edition.