Chapter Nine

The Challenge of Diabetes Mellitus:
The Urgent Need for Life style Modification

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Acknowledgement

I am most grateful to Allah, the creator and sustainer of the universe for all the favours HE has bestowed on me and for allowing us to witness this event. I am also grateful to the Vice Chancellor, Professor Abdullahi Mustapha FPSN and the University Inaugural lecture committee for the opportunity to deliver this inaugural lecture; an opportunity for me to share my experiences as a physician, and academician.

I must also appreciate the contributions of my great teachers, colleagues, students and most importantly patients without whose contributions; I would certainly not be in a position to deliver this important lecture. I am particularly grateful to my great teacher and mentor; Professor G.C. Onyemelukwe for his invaluable contributions and tutelage. I am also grateful to all staff of the Department of Medicine past and present for their individual and collective contributions. Particular mention must however be made of Professor Ibrahim Abdu-Aguye, Professor J.U Okpapi, Professor SS Danbauchi, Professor Abdullahi Abba, Professor Balarabe Sani Garko the current Head of department, Dr (Mrs) FE Anumah, Dr Fatima Sani Bello, Dr Mohammed Sani Isa, Dr Albert Oyati, Dr IB Bosan, and Dr A Ibrahim among others.

I am also grateful to all my students both undergraduate and postgraduate for the constant challenge they pose for me to continue to be intellectually relevant. My patients, through their trust and sacrifice were the most important assets that catalyzed my intellectual sojourn; and I would remain eternally grateful to all of them.

I am eternally grateful to my dear parents for the discipline and training they inculcated in me. I am grateful to my biological brothers and sisters especially Dr Salihu Bakari (*Wakili-Makaranta* Adamawa) for their invaluable support, understanding and contributions. My gratitude knows no bound to my spouses especially Hajiya Maryam (Yerima Maiha) and my children who sacrificed everything for me to succeed.

Prologue

> *"No human ever filled a container more evil than his belly. The few morsels needed to support his being shall suffice the son of Adam. But if there is no recourse then one third for his food, one third for his drink and one third for his breath." (Muhammad Rasulullah SA.W. as reported by Ahmad and At-Tirmidhi).*

> *The person who passes urine which is exceedingly sweet, cool, slightly viscid, turbid, and resembling the juices of the sugarcane . . . suffers from glycosuria....There are two types of urinary disorders—one, natural due to genetic factors, and the other due to indiscreet living or dietetic indiscretions. The patient suffering from the former is thin, pale, eats less and drinks too much.... The patient with the latter is usually obese, eats a lot, is stout, of sedentary habits and sleeps too much. (Charaka Samhita and Sushnita Ayurveda, 100-200BC).*

It is indeed a great honor to stand before you this afternoon to deliver this inaugural lecture on behalf of the Department of Medicine. This would be the third inaugural lecture from the Department after the ones delivered by my great teacher and mentor Professor Geoffrey C. Onyemelukwe in 1997 and more recently my brother, friend and current Head of Department; Professor Balarabe Sani Garko in February 2014.

The Vice-Chancellor Sir, distinguished ladies and gentlemen, the title of my lecture today seems too obvious to even the most ordinary of minds. I had thought of many other titles such as "the bitter side of Sugar", "the price of over indulgence" "starvation in the midst of plenty", and "Moderation; the Key to Life" for this lecture, but settled on "The Challenge of Diabetes Mellitus: An Urgent Need for Life Style Modification." As diabetes

is a household name today in our community affecting the rich and poor alike.

As a Physician, my training has been and would continue to be the application of scientific knowledge to appreciate and maintain balance between extremes. This critical balance between extremes is what is regarded as "normal" in the general parlance. Hence we talk of a normal height (not too tall and not too short), normal weight (not fat or lean), a normal blood pressure (not low or high), normal blood sugar (not low or high) etc. It therefore follows that for all attributes, activities, functions there is what is considered normal or abnormal variation.

The Vice-Chancellor Sir, I intend to take us through a malady that is threatening mankind with extinction if urgent measures are not taken to control it. This malady results from the breakdown of glucose regulation which to a large extent has been occasioned by our failure to moderate our lives. I would be sharing our experiences on the challenge posed by diabetes mellitus.

Introduction

Diabetes mellitus a multifaceted, heterogeneous and a multifactorial metabolic disorder is characterized by chronic hyperglycaemia.[1-7] The term diabetes mellitus is derived from two Greek words *diabetes* meaning siphon (i.e. that which passes through) in Greek; and *mellitus, which* is a Greek word for sweet. *Mellitus* also means honey in Latin. The term diabetes was first used in the second century to describe the condition based on the two most common symptoms i.e. excessive thirst and excessive urination[5]. The urine of these patients tastes sweet and hence the addition of the adjective *mellitus*.

Diabetes mellitus is not a single disease, but several disease conditions that manifest with hyperglycaemia (the hallmark of diabetes mellitus) as the final common factor. [1,8,9] Chronic (prolonged) hyperglycaemia results from several and diverse disease processes, which leads to either total; or relative deficiency of insulin (a hormone secreted from the pancreas that helps body cells to utilize glucose). The deficient action of insulin is associated with disturbances in the ability of the body to utilize the major food classes utilized by the body namely: carbohydrate, fat and protein. It arises when the pancreas fails to produce enough insulin (type I

diabetes), or when the body cannot promptly secrete and or effectively make use of the insulin produced (type 2 diabetes).

There is evidence that there were descriptions of diabetes in Egypt as early as the 15th century BC[4]. Similarly, Avicenna the famous 11th century Arab clinician, has to his credit detailed descriptions of diabetes mellitus in medical literature. Although diabetes existed for quite a long time, it was however quite rare then. It has been stated that Galen saw only two cases of diabetes in his entire medical career[5]. Similarly, the existence of the disorder in Africa was extremely rare[10].

Although diabetes mellitus has been in existence from time immemorial, the incidence (number of new cases occurring in a given population per-year) and prevalence (proportion of a given population with the condition at a particular point in time) have exponentially increased, and continues to rise in a global scale. In other words, it is now a pandemic. Its prevalence estimated at 150 million people in 2001 increased to 382million in 2013, and is expected to exceed 471million by the year 2035. [6,7] This is due to a mixture of factors such as progressive increase in population size, increased proportion of older adults in the population and most importantly unhealthy lifestyles. The prediabetic state of impaired glucose tolerance and impaired fasting glucose are even more prevalent than diabetes itself, meaning that the future is even more bleak, if urgent steps are not taken to reverse this ugly trend.

Quite unfortunately, and most importantly for us; the rapid increase in the incidence and prevalence of diabetes mellitus has been more dramatic in developing countries; places that could least afford the cost implications of these changes both in terms of human and material resources. Fortunately however, preventive measures are practicable and have been shown to be the most cost-effective method in the control of this menace that threatens the very existence of mankind.[10, 11]. This however requires appropriate knowledge by all and sundry, but more especially policy makers, diabetic individuals and their relatives; and indeed all health workers.

Normal Carbohydrate Metabolism

To properly appreciate diabetes mellitus, there is the need to appreciate the processes that normally take place in the day-to-day

routine of eating and fasting. It is well appreciated that we are not always eating, but eat a specified number of meals every day; in between which the energy requirements for the normal day-to-day activities are supplied from our storage pools.

In other words, there are feast periods interspersed with periods of fasting. The excess energy consumed during the feast period is stored to be utilized during the fasting period.

There are basically three main classes of macronutrients; namely carbohydrates, proteins and fats. These are however too complex to be absorbed by the intestinal lining (***mucosa***). After the process of digestion (a complex process that involves both enzymes and mechanical factors) however, carbohydrates are broken down to simpler sugars mainly glucose. Proteins are broken down to amino acids and fats are broken down to fatty acids and glycerol. These simpler compounds are easily absorbed by the intestinal mucosa and through the blood circulation (***portal circulation***) reaches the pancreas, the liver and the general (***systemic***) circulation.

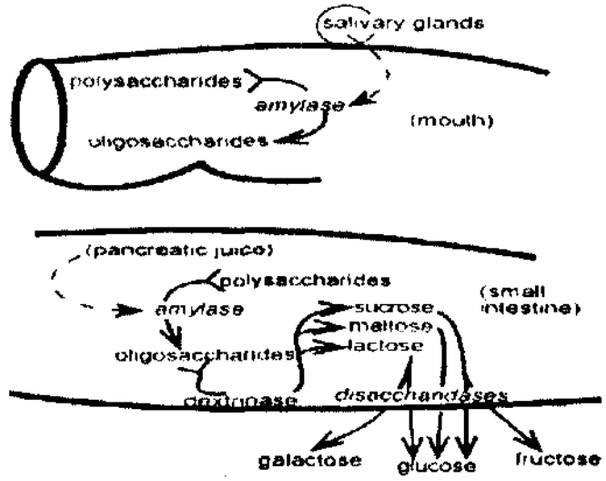


Figure 1: Digestion of Carbohydrates.

Following a meal, glucose derived from food appears in the systemic circulation within as early as 5 to 10 minutes. [13,14] In the pancreas, the resultant increase in portal plasma glucose and amino acids stimulates the secretion of ***insulin*** and suppresses the secretion

of ***glucagon*** (a hormone in the pancreas that does the exact opposite of insulin). The resultant rise of plasma insulin level in the portal circulation leads to several events. These events are sometimes referred to as ***anabolic*** (body building) actions of insulin. These anabolic actions of insulin are:

i. Conversion of glucose to glycogen which is then stored in the liver and skeletal muscle for use when nutrients are deficient.(as much as 40% of glucose derived from food is eventually taken up by the liver)
ii. Blockage of liver output of glucose (prevention of glycogenolysis), hepatic glucose production is suppressed by as much as 60 %.
iii. Storage of fatty acids and glycerol in fat cells and inhibition of breakdown of fat (prevents lipolysis).
iv. Prevention of break down of muscles and stimulation of storage of amino acids as proteins in skeletal muscles.

When blood glucose levels decline, pancreatic secretion of insulin follows suit, on the other hand; pancreatic secretion of ***glucagon*** rises. The sole function of glucagon is to do the exact opposite of what insulin does, i.e. to increase blood glucse levels and avoid hypoglycaemia (low blood glucose levels) this it does by stimulating the liver to produce glucose by breaking glycogen (glycogenolysis). However,when fasting exceeds 12-15 hours, depletion of hepatic glycogen stores occurs resulting in increase in the rate of gluconeogenesis (production of glucose from other sources usually protein) to make up for tissue demands. These processes are aimed at maintaining a tight control on blood sugar such that it is neither high nor low and maintain glucose levels within the normal range in normal individuals. This is important, as glucose is the single most important fuel in the body with out which the brain cannot function for more than 5 minutes. It is also noteworthy that other hormones such as adrenalin, thyroid hormones, corticosteroids, and growth hormone all exhibit effects similar to that of glucagon on glucose homeostasis and are actually brought to action under situations of biological stress.

Insummary,starches are digested in the gut from where they enter the blood stream in the form of glucose. Figure 2 below

summarises the respective roles of insulin and glucagon in glucose homeostasis.

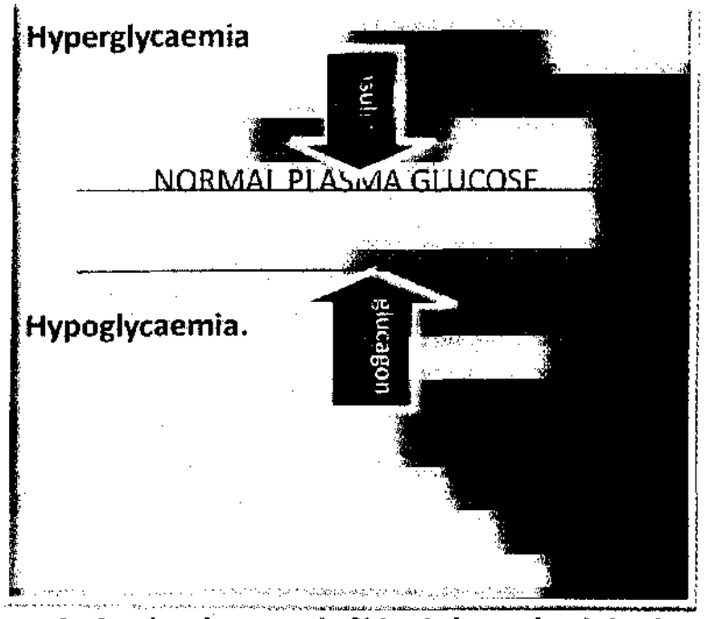


Figure 2: showing the control of blood glucose levels by the main hormones of glucose control

The glucose in the blood stream becomes a potential source of energy for the entire body, similar to the way in which petrol is a potential source of energy for your car. Similarly, just as the petrol in the tank of the car needs to be pumped into the car engine to be of any effect, the body requires some assistance to get glucose from the blood stream to the muscles and other tissues of the body. In the body, that assistance comes from a hormone called insulin. Without insulin, glucose cannot get into the cells to be used as fuel. Instead, it accumulates in the blood to high levels and is excreted or "spilled" into the urine through the kidneys once the renal threshold (usually 10mmol/L) is exceeded.

Glucose Intolerance

When blood glucose levels are persistently elevated above normal, glucose intolerance is said to be present, diabetes mellitus

being the worst form of it. Although the pathogenesis of type 2 diabetes is not fully understood, there appears to be a transitory intermediate state between normoglycemia and type 2 diabetes. The World Health Organization (WHO) in 1999 recognized the presence of two transitory intermediate states as separate classes of glucose intolerance. These intermediate states are; impaired fasting glycaemia (IFG), and impaired glucose tolerance (IGT). These states (IGT and IFG) are termed prediabetes. According to International Diabetes Federation (IDF)/WHO criteria, IFG is defined as fasting plasma glucose (FPG) of 6.1 to 6.9 mmol/l while the American Diabetes Association (ADA) criteria define it as a FPG of 5.6 to 6.9 mmol/l. On the other hand, IGT is defined as plasma glucose concentration of 7.8 to 11.0 mmol/l after a two-hour 75g (anhydrous) oral glucose load, referred to as Oral Glucose Tolerance Test (OGTT).[15]

Impaired fasting glycaemia (IFG)

When fasting plasma glucose levels are above 6.0mmol/L (110mg/dl) but less than 7.0mmol/L (126mg/dl) the cut off point for the diagnosis of diabetes, impaired fasting glycaemia is said to be present. It is important to investigate such individuals further by requesting post-prandial blood glucose (preferably a 2-hour post prandial blood sugar); if the values are indeterminate, an OGTT may be prudent to properly classify the type of glucose intolerance.

Impaired Glucose Tolerance (IGT)

IGT is diagnosed when a 2 hour plasma glucose after an OGTTT is $\geq$ 7.8 mmol/l (140mg/dl) but less than 11.1mmol/l (200mg/dl) the cut off point for the diagnosis of diabetes. Although not all individuals with IGT develop diabetes, approximately one in three individuals with IGT will develop type 2 diabetes within 10 years if left untreated, suggesting that they are at increased risk and therefore a potential intervention target group. Although IGT itself is not diabetes, it however carries a significant risk of large vessel disease such as strokes, heart attacks and peripheral vascular disease.

Classification of Diabetes Mellitus

The current classification of mellitus is summarized below[1].

- ❖ Type 1 (1a, 1b)
- ❖ Type 2 Diabetes.
- ❖ Gestational Diabetes.
- ❖ Secondary Diabetes.

Type 1 Diabetes

Type 1 Diabetic patients have little or no endogenous insulin secretory capacity, and therefore require insulin therapy for survival. There are two main forms of clinical type 1 diabetes designated types 1a and b.

Type 1a

This form of type-1 diabetes results from immunologic destruction of pancreatic ß cells as a result of auto-immunity. The susceptibility and trigger factors are not clear but both genetic and environmental factors play significant role. Type 1a is characterized by the presence of islet cell antibodies (ICA), anti-glutamic acid decarboxylate (anti-GAD), IA-2 or insulin antibodies that helps to point at the autoimmune process. The rate of pancreatic ß cell damage varies from one individual to another; when 80% to 90% of pancreatic ß have been destroyed clinical diabetes develops as a result of insulin deficiency. However, it is also possible to have features of diabetes in the event of stressful conditions such as acute infections even when the beta-cell reserve is much higher than this. In these circumstances, normoglycaemia may resume after the acute stress have abated only to reappear when the critical level of destruction of the beta cell has occurred. This is the so called honey moon period, and such patients should not be confused with type-2 diabetic patients.

About 90% of type 1 cases in Europe manifest type1a diabetes and show evidence of auto-antibodies in their sera. In Africa however, the proportion of type-1 in this category is likely to be less than what has been observed in Europe as autoimmune disorders are generally less prevalent probably as a result of the interactions between the immune system and several infections and infestations like malaria.

Type 1b

In type 1b on the other hand, there is no evidence of autoimmunity and hence called idiopathic and constitute about 10% of type 1 diabetes in Europe. To date, there is no known etiological basis for type 1b diabetes mellitus. Some of these patients have permanent insulinopaenia and are prone to ketoacidosis, but have no evidence of autoimmunity. This form is more prevalent among individuals of African and Asian origin and may indeed be some form of type-2 diabetes or poorly characterised secondary diabetes from primary beta-cell failure[1].

Type 2 diabetes

Type 2 diabetes is the commonest form of diabetes and is characterized by disorders of insulin secretion and insulin resistance. Globally, it affects about 5-7% of the world's population. This prevalence is underestimated because many cases, perhaps 50% in some population, remain undiagnosed[7].

Gestational Diabetes mellitus

Gestational Diabetes mellitus (GDM) refers to the onset or initial recognition of glucose intolerance during pregnancy, usually in the second or third trimester. A clear distinction should be made between this class and a pregnant diabetic patient, this would however be possible after the peuperium.

Secondary diabetes

Secondary diabetes is said to be present when an identifiable cause has been established as the cause of diabetes. The causes of secondary diabetes include genetic defects of the pancreatic ß cell or genetic defects in the pathways of insulin action such as insulin receptor mutations or post-receptor defects. Also included are diseases of the exocrine pancreas such as pancreatitis and disorders of endocrine glands producing excessive insulin counter regulatory hormones such disorders include thyrotoxicosis, Cushing's syndrome, acromegaly, phaeochromocytoma etc. Also known to cause secondary diabetes are certain drugs such glucocorticoids, pentamidine, reverse transcriptase inhibitors, and α-interferon. We have reported the first case of diabetes mellitus resulting from anti-retroviral therapy in West Africa.[9]

The Epidemic of type-2 Diabetes

There has been progressive increases in the incidence and prevalence of type 2 diabetes worldwide, this is particularly so in underdeveloped, and developing countries. . Its prevalence estimated at 150 million people in 2001 increased to 382million in 2013 is expected to exceed 471million by the year 2035. [6, 7] In 2013, 5.1 million people died of diabetes meaning 10 people died every minute from diabetes in 2013. Equally worrisome is the fact that the epidemic affects mainly those aged between 40-59 years of age especially in the developing countries implying that the productive members of the society are lost with resultant negative effects on the economies of these countries. Diabetes indeed led to at least 548 billion United States Dollars in direct health care costs (about 11% of total health care spending on adults)[7]. More worrisome is the fact that 80% of diabetics live in low and middle income countries. Place of residence is a major determinant of DM in sub-Saharan Africa with urban residents having higher prevalence of DM than their rural counterparts. In low and middle income countries, the number of people with DM in urban areas is 172 million, while 119 million live in rural areas. By 2030 the difference is expected to widen with 314 million people living in urban areas and 143 million in rural areas[7].This is attributable to lifestyle changes associated with urbanization. Changes in lifestyles such as excessive intake of calories (usually refined foods), decreased physical activity leading to sedentary lifestyles as a result of modernization as well as genetic factors are responsible for this change.

The Role of Genes

Familial clustering and high concordance rates among monozygotic (identical) and dizygotic (non-identical) twins argue strongly for a role of genetic factors in the aetiology of type 2 diabetes [16,17] . In a prospective study of 2,322 Swedish men, 1,860 of whom turned up for follow-up 7 to 14 years later, the incidence of diabetes rose from 3% among those who had no close relative with diabetes to 16% among those with two or more diabetic relatives (more than fivefold increase). [16] Furthermore, the prevalence of diabetes among parents or siblings was found to be at least twice among those who developed diabetes when compared to those who did not develop diabetes. Despite these suggestions of a probable

role of genetic factors in the causation of type 2 diabetes, the actual gene or genes that are important in the causation of type 2 diabetes mellitus however remains elusive. It is most probable that the genes that are inherited increases tendency to the development of tye-2 diabetes when other environmental factors are favorable, in other words, they play a permissive role in the causation of type-2 diabetes.

The Role of Modifiable Environmental Factors

Environmental factors provide the necessary conditions for the development of type 2 diabetes mellitus given the right genetic environment. Established acquired risk factors for the development of type 2 diabetes include ***obesity*** ***increasing age***, ***physical inactivity***, and ***urbanization*** [19-22].

Obesity

Excessive weight is probably the most important modifiable acquired risk factor in the aetiology of type 2 diabetes found in many cross sectional and longitudinal studies. It has been stated that 50% of the diabetic epidemic in the developing world could be reversed simply by controlling the scourge of weight gain in these communities[17]. To define the degree of obesity, the body mass index (BMI) is calculated by dividing body weight (in kilograms) by the square of the height (in meters) [18]. Based on BMI, individuals may be classified as follows:

- Underweight = BMI < 18.5
- Normal weight. = BMI 18.5 -24.99
- Preobese = BMI 25.0-29.99
- Obese class I = BMI 30.0 – 34.99
- Obese class II = BMI 35.0 – 39.99
- Obese class III = BMI > 40.0

In a prospective study involving a cohort of healthy Swedish men, followed up for the development of type 2 diabetes mellitus, the incidence of diabetes mellitus rose by a factor of twenty-two when individuals with the highest BMI were compared with those who had the lowest BMI[15]. Similarly, a prospective study involving more than 7000 British men (mean follow-up of 12.8 years) established a strong positive correlation between a high BMI and the

development of type 2 diabetes. [17] These observations are expected as obesity is known to induce insulin resistance

Aging

Although not modifiable, increasing age is known to be associated with insulin resistance[19]. This implies that with increasing age, "risky lifestyles" are more likely to result in the development of diabetes mellitus.

Sedentary life styles

Sedentary life have been shown to be a significant risk factor for the development of type 2 diabetes and regular moderate exercise reduces the risk of type 2 diabetes by improving insulin sensitivity[20,21]. More than 50% reduction in the risk of development of type 2 diabetes has been reported by moderately vigorous exercise in the British study referred to above.

Role of Urbanization

Urbanization has been shown to significantly increase the risk of development of type-2 diabetes[22]. This could be due to life-style changes such as increased caloric intake usually in the form of junk foods containing dense calories, increase use of machinery and therefore less tendencies to physical exertion with consequent weight gain could partially explain this trend. In Africa, Urban lifestyle is characterized by changes in dietary habits involving an increase in the consumption of refined sugars, saturated fat, and reduction in fiber intake. Urbanization tends to decrease physical activity as very little physical activity is required for daily living whereas rural populations rely on foot walk as transportation means and often have intense agricultural activities as their main occupation. Furthermore psychosocial stress associated with urbanization may also contribute to this increased risk. It is interesting to note that more recently; the stress attributable to shift work has been shown to be positively associated with the risk of developing type-2 diabetes[23].

Role of intra-uterine and early childhood events

There are suggestions that in the hunter-gatherer life-style of our predecessors genes were acquired to enable the storage of

energy in the form of fat in adipose tissue[24]. By encouraging the storage of energy, energy supply during periods of food shortage is guaranteed. This was a definite advantage to ensure survival. In the setting of affluence however, these genes continue to promote energy storage, which results in obesity which in turn induces insulin resistance and glucose intolerance. This is referred to as the thrifty genotype hypothesis. In support of this hypothesis, are observations among Pima Indians of Arizona, USA. In that population, dramatic changes in life-styles from the traditional form, characterized by low caloric intake as well as demands of more strenuous physical activity to a more sedentary form associated with excessive consumption of calories resulted into high rates of obesity, glucose intolerance and type 2 diabetes mellitus. Conversely, a sister tribe of the Pima Indians residing in northern Mexico still maintains the traditional life-styles and has lower rates of obesity and type 2 diabetes[21].

An alternative "thrifty phenotype" hypothesis on the other hand, suggests that environmental constraint on fetal growth such as intra-uterine malnutrition results in adaptive changes in the development of some organs in the feotus[25]. This is aimed at preserving the growth of certain organs considered essential to survival of the fetus. Such organs include the brain at the expense of others such as the viscera. The resultant changes lead to under development of the endocrine pancreas and the liver, leading to reduced capacity for insulin secretion and insulin resistance respectively. This leads to increased susceptibility to type 2 diabetes in adult life. This hypothesis is supported by epidemiological observations that consistently demonstrated associations between indices of poor fetal and infant growth with susceptibility to glucose intolerance in adult life. In a follow up study of 468 British men born between 1920-1930 whose birth weights were known, Hales and coworkers found that plasma glucose levels at 30 minutes and two-hours during OGTT were inversely proportional to birth weights[26]. Furthermore, the rate of impaired glucose tolerance increased with lower body weight at one year (26% among those weighing 8.16 Kg or less at the age of one year versus 13% among those weighing 12.25 Kg or more at one year of age).

Similarly, the Nurses' Health Study[27], involving a cohort of 121,701 United States women born between 1921 and 1946

concluded that birth weight is inversely associated with risk of development of type 2 diabetes mellitus.

Pathogenesis of type-2 Diabetes

Type-2 diabetes mellitus is a heterogeneous metabolic disorder characterized by chronic hyperglycaemia due to dynamic interactions between varying defects of insulin secretion and insulin resistance. Insulin resistance refers to the inadequate response of the skeletal muscle, liver, and adipose tissue to the endogenous insulin secretions. In addition to insulin resistance, β-cell dysfunction plays an integral role in the pathogenesis of T2DM. In healthy individuals, β-cells can reverse insulin resistance by increasing the production and secretion of insulin. Glucose sensors located on β-cells sense the rising blood glucose levels despite high insulin secretion. Either of these defects may be the predominant feature in a particular case [28-31]. There is considerable debate and controversy as to whether it is insulin resistance or pancreatic beta-cell failure that initiates the cascade of events that culminates into type-2 diabetes. Whereas Martins *et al* [29] established that insulin resistance is the primary defect that precedes the development of type 2 diabetes mellitus, Banerji and Lebovitz noted that about 59 % of African-American type 2 diabetic patients do not exhibit insulin resistance even when diabetes is already manifest, [30] suggesting that pancreatic beta cell failure may be the predominant, if not the sole defect in a good number of type-2 diabetic African-Americans. We studied the pancreatic beta-cell function in type-2 diabetic patients in Zaria[32] using the homeostasis model assessment (HOMA) developed by Matthews *et al* [33].

In this model, the results of the computer-derived estimations of beta-cell function as a percentage of expected beta-cell function in lean young adults are the same as the values obtained from the simple mathematical equation below.

$$\textit{Percent beta-cell function} = 20 \times \frac{\textit{fasting plasma insulin(micro-units/L)}}{\textit{Fasting plasma glucose (mmol/L)} - 3.5}$$

In this study, we have demonstrated that type 2 diabetic Nigerians of Hausa-Fulani ethnicity exhibit much lower pancreatic beta cell function compared to control subjects.

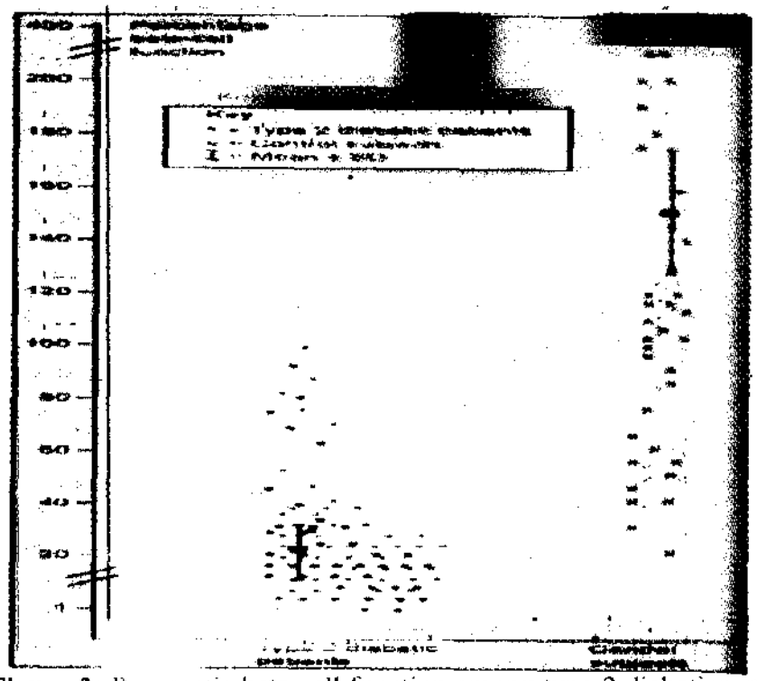


Figure 3: Pancreatic beta cell function among type-2 diabetics and controls in Zaria

This finding is expected, and similar to earlier findings elsewhere[28, 31, 33-35]. Studies in South African blacks suggest an early pancreatic beta-cell failure as the operative defect in black type-2 diabetic patients, which lead Joffe and Seftel [35] to postulate a decrease in the mass of functioning beta cells as a key factor. In our study however, it is impossible to suggest whether the observed pancreatic beta-cell failure is the cause of or is the result of type 2 diabetes mellitus, since it is known that hyperglycaemia causes as well as aggravate pancreatic beta-cell secretory failure[34]. However, since few of the control population demonstrated evidence of pancreatic beta-cell dysfunction (8.3% showing beta-cell function less than 50% of reference value), suggesting probable decreased beta-cell mass; an argument for the role of pancreatic beta-cell failure as the underlying defect in type 2 diabetes mellitus in this environment could be advanced. It is rational to assume that those with low beta-cell mass are likely to develop diabetes when challenged with the stress of urbanization and modernization, such

as sedentary life-styles, excessive calorie consumption and the attendant obesity all stressors that would lead to insulin resistance which an individual with low pancreatic beta-cell mass may not be able to cope with. Indeed this hypothesis is in tandem with our previous findings of low insulin levels both in the fasting state and in response to oral glucose challenge among the same population of patients[4]. It is also consistent with our observation that type-2 diabetic patients in this environment require insulin much earlier than reported in western literature (unpublished observation). On the other hand, we used the HOMA method to compute insulin resistance in 40 type-2 diabetic subjects and 36 controls. We found that the mean HOMA scores were significantly higher among type 2 diabetic subjects than controls. Ten (27.8%) of the control subjects demonstrated HOMA insulin resistance values greater than one compared to 35 (87. 5%) type-2 diabetic patients ($p<0$ .05). we concluded that although type-2 diabetic patients' in this study exhibit more insulin resistance than control subjects, insulin sensitive variants of type-2 diabetes is also found in our population.

Aetiology of Type 1 Diabetes

Type 1 diabetes results from autoimmune destruction of pancreatic beta cells. Like type 2 diabetes, its causation depends on both genetic and environmental factors [36-38].

Role of genes

Known susceptibility genes for type 1 diabetes are located in the immune response genes HLA. The common ones are HLA DR3 and HLA DR4 [36]. European populations are known to have higher rates of these genes compared to Negroid races. This may partially explain the relative lower incidence of type 1 diabetes in the latter compared to the former. However, it is important to note that the presence of the genes alone do not result in type 1 diabetes. An appropriate environmental stimulus is required to work in concert with the genes before type 1 diabetes becomes manifest.

Role of Environmental Factors

Genetic factors alone cannot explain the rapid rise in the prevalence of type 1 diabetes in the last 50 years or so. Several environmental factors have been implicated most of the agents

implicated are thought to act by the process of antigenic mimicry. Main factors implicated are viral infections e.g. Cocksackie B4, mumps, congenital rubella; and the role of early infant feeding with artificial formulas containing cow milk [37,38]. Cow milk universally contains Bovine serum albumin (BSA), which exhibits antigenic similarity with protein p69 of pancreatic beta cells leading to autoimmune serological and cellular reactions culminating in beta cell destruction[38].

Parasitic infestations are known to suppress auto-immunity and could partially explain the relative rarity of autoimmune disorders including type 1 diabetes in the tropical environment where parasitic infestations are endemic.

Pathogenesis

In a susceptible individual, an immune mediated destruction of the pancreas is initiated by an environmental event. This results in the reduction of total beta cell mass and a proportional increase in activity in normal beta cells to compensate for the deficiency. However, the increased activity renders the normal cells more susceptible to autoimmune destruction. Symptoms of diabetes mellitus become manifest when 80% to 90% of beta cells have been destroyed[36,37].

Clinical Presentation of Diabetes Mellitus

Individuals with diabetes mellitus present to the clinician in different ways, and up to half of diabetic patients may have no symptoms and are diagnosed incidentally[7]. Basically diabetic patients present for the first time to the clinician in one of the following scenarios.

i. During routine investigations (without any symptom).
ii. Patients seeking medical attention because of symptoms of diabetes with or without symptoms of diabetic complications (discussed below).
iii. Sometimes individuals may present with symptoms of one or more complications of diabetes.

Symptoms of Diabetes Mellitus

The following quotation from the ancient Indian literature probably gives the best description of the major symptoms of

diabetes mellitus. ***"The person who passes urine which is exceedingly sweet, cool, slightly viscid, turbid and resembling the juices of sugar cane. Suffers from glycosuria..There are two types. One due to genetic factors. The other due to indiscreet living or dietary indiscretions. The patient suffering from the former is thin, pale, eats less and drinks too much The patient with the latter is often obese eats a lot, is stout of sedentary habits and sleeps too much." Charka Samhita and Sushinita Ayurveda circa 100-200 BC.***

Although the symptoms of diabetes are protean, diabetic patients usually complain of the following symptoms at diagnosis.

Polyuria

This is technically defined as passage of more than three liters of urine per day. Polyuria results from the osmotic effects of glucose and other solutes e.g. ketone bodies that should normally be reabsorbed by the kidney tubules after filtration. When the absorptive capacity of the kidney is exceeded, i.e. when the renal threshold for these solutes has been surpassed (renal threshold for glucose is 10mmol/L or 180mg/dL), the excess is lost in the urine. Since these substances are osmotically active, water loss by the kidney tubules compulsorily accompanies their excretion. The result is excessive amounts of urine both during the day and at night.

Polydipsia

Polyuria results in net extra cellular fluid loss leading to dehydration and increase in serum osmolarity. To compensate for the excessive water losses in urine and to the high serum osmolarity occasioned by high levels of glucose in the blood and dehydration, the thirst centre is stimulated. This centre is situated at the anteromedial hypothalamus and is sensitive to small changes in osmolality (normally 290-300 mOsm/L).

Polyphagia

In the diabetic state, although there are excessive amounts of glucose in circulation, there is defective utilization of glucose and the other fuels such as protein and fat by insulin sensitive cells. As far as these cells are concerned therefore, there is a state of insufficient utilizable fuels in the system. In other words, there is

starvation in the midst of plenty. This leads to increased appetite to meet up with the supposed state of starvation.

Weight loss

As a result of insulin deficiency (relative or absolute) insulin sensitive cells are not able to utilize the basic source of energy notably glucose effectively. This result in the use of alternative sources of energy notably fat deposited in fat cells; and amino acids stored in the form of protein in skeletal muscle. Fat cells and skeletal muscle are broken down. However, even the energy from these alternative sources is not utilized efficiently in the setting of insulin deficiency in other words the energy also gets "misappropriated". Furthermore more and more of these precious sources of energy are lost in the urine leading to a net loss in total energy balance. The result is progressive weight loss despite good appetite.

Recurrent infections

Diabetic patients are more susceptible to both acute and chronic microbial infections as a result of defects of cell mediated and humoral immunity, as well as defective phagocyte function. These defects have a direct correlation with glycaemic control and improve with improvement in glycaemic control. Diabetic patients may present for the first time with recurrent infections.

Eye symptoms

Visual symptoms range from blurred vision to outright blindness and are usually due to high or rapidly changing levels of blood sugar, opacification of the lens (cataract) or retinopathy.

Impotence

Sexual problems are highly prevalent and bothersome for the diabetic person. In fact it may be the main reason for the consultation, and only after careful clinical evaluation; would the underlying diagnosis of diabetes be obvious. Impotence or more appropriately referred to as erectile sexual dysfunction in the male is a common complain among diabetics.

Poor Obstetric History

Women with diabetes experience reproductive abnormalities such as delayed menarche and increased incidence of menstrual

cycle irregularities as well as delayed ovulation leading to reduced fertility rates. Furthermore, they are at increased risk for recurrent abortions, and history of large healthy looking babies with neonatal deaths.

Foot sepsis/gangrene

Diabetes is the leading cause of non-traumatic lower extremity amputation. Diabetes foot sepsis may be the initial presenting feature of diabetes. Typically, this complication starts spontaneously with blisters occasionally following trivial trauma.

Loss of consciousness

Loss of consciousness could result from an acute complication of diabetes such as diabetic keto-acidosis, hyperosmolar non-ketotic coma or as a result of complications of therapy such as hypoglycaemia and lactic acidosis

Diagnosis

On the basis of data from three different populations aimed at identifying the fasting blood glucose levels that best predicted the risk of developing micro vascular complications, the ADA approved new diagnostic criteria for diabetes mellitus on the basis of recommendations from an expert committee in 1997. These criteria are symptoms of diabetes and a casual plasma glucose concentration of ≥11.1 mmol/l (≥200mg %) or a fasting plasma glucose value of ≥7.0 mmol/l (≥126mg %) or 2 hour plasma glucose value of ≥11.1 mmol/l (≥200mg %) during a standard 75 g. The WHO accepted these criteria in 1999. For clinical diagnosis, a second test is recommended for confirmation, while for epidemiological studies, the use of fasting plasma glucose levels of 7.0 mmol per liter alone is acceptable[1].

Complications of Diabetes

For the sake of convenience, it is easier to look at diabetic complications from the temporal point of view. Thus we talk of acute complications, which occur relatively over a short time frame, potentially life threatening; and may be precipitated suddenly by such factors as infections, psychosocial stress, injuries or side-effects of drugs used for the management of hyperglycaemia. Such

complications include diabetic keto-acidosis (DKA), hyperosmolar non-ketotic coma (HONK), lactic acidosis and hypoglycaemia.

On the other hand, chronic complications tend to occur over a relatively longer time frame, as prolonged hyperglycaemia appears to be required in their pathogenesis. Chronic complications are typically insidious in onset but relentlessly progressive unless metabolic control is achieved and maintained. However, it is important to note that since type-2 diabetes is typically asymptomatic in a large proportion of individuals and therefore undetected, chronic complications of diabetes may be the first manifestation of the condition.

Chronic Diabetic Complications

Not all patients with diabetes develop chronic complications regardless of their metabolic control. On the contrary, some patients develop chronic complications quite early even in the presence of only "mild" elevations of blood sugar levels. To explain these extremes, two hypotheses have been advanced. The metabolic hypothesis presupposes that chronic diabetic complications are as a consequence of hyperglycaemia in other words no hyperglycaemia no complications and the rates of their development are directly proportional to plasma glucose levels. The genetic hypothesis on the contrary considers diabetic complications as a result of the same gene(s) that caused diabetes in the first place in other words complications would occur irrespective of the level of glycaemic control. However, a midway hypothesis is most likely to be true rather than either of the first two hypotheses. This hypothesis suggests that while susceptibility to diabetic complications varies between patients, chronic hyperglycaemia appears to be a prerequisite for the development of these complications. Findings from the Diabetes Complications and Control Trial (DCCT) [41], a multi centre study involving 1441 type 1 diabetic patients from 28 centers followed up for 5-10 years has conclusively demonstrated that tight glycaemic control reduces the risk of retinopathy and nephropathy in the case of type 1 diabetes. Similarly, the United Kingdom Prospective Diabetes Study (UKPDS) [39] in the case of type 2 diabetes strongly supports this midway hypothesis.

The traditional chronic complications of diabetes are

- Neuropathy.

? Angiopathy
? Retinopathy
? Nephropathy.
? Diabetic foot.
? Musculoskeletal.

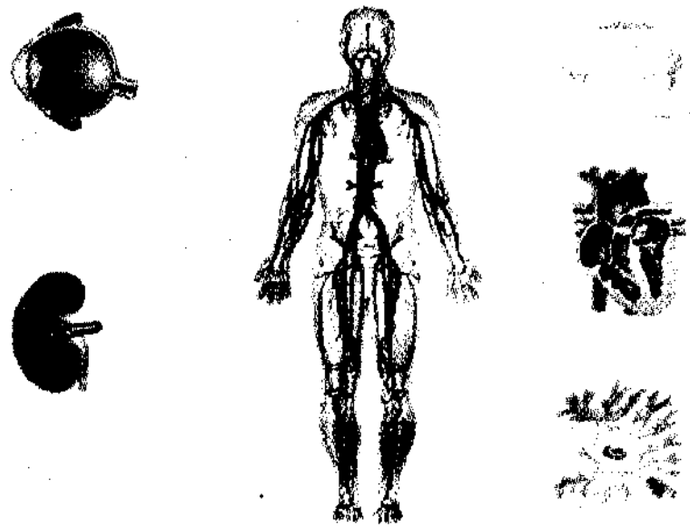


Figure 4: Systems affected by chronic Diabetic complications

Neuropathy

Peripheral and autonomic nerves are variably affected in diabetes mellitus and the consequent metabolic changes. This results in functional disturbances and pathologic changes in the nerves with resultant clinical symptoms and signs. Diabetic neuropathies present in several ways and are of varying severity.

Angiopathy

Atherosclerotic disease accounts for most of the excess mortality in patients with diabetes. In the UKPDS, fatal cardiovascular events were 70 times more common than deaths from

microvascular complications. The relationship between glucose concentrations and macro vascular events is less powerful than for microvascular disease; smoking, high blood pressure, proteinuria, and cholesterol concentration are more important risk factors for large vessel disease in patients with diabetes. The large vessel diseases present as ischaemic heart disease, peripheral vascular disease or cerebrovascular disease. Cerebrovascular disease could lead to acute brain infarction also known as stroke.

Stroke

The risk of thrombotic stroke is two to three times higher in patients with diabetes, but the rates of haemorrhagic stroke and transient ischaemic attacks are similar to those observed among the non-diabetic population. Patients with diabetes are more prone to irreversible rather than reversible ischaemic brain damage, and small lacuna infarcts are common. Unfortunately, stroke patients with diabetes have higher death rates, poorer neurological outcome and consequently more severe disability. However, maintaining good glycaemic control immediately after a stroke is likely to improve outcome although long-term survival is reduced due to high recurrence rates.

Visual Impairment

Eleven percent (11%) of community-dwelling adults with diabetes have impaired vision. This could be as a result of cataracts, refractive errors or retinopathy.

Retinopathy

Involvement of the retina is referred to as retinopathy; and it is a common complication of diabetes. Diabetic retinopathy is the principal cause of blindness in the adult population of most technologically advanced societies where it is adjudged the commonest cause of blindness in people aged 30-69, and by the year 2035 if the trend remains unchecked, it would be commonest cause of blindness globally[7]. Estimates of the prevalence of retinopathy vary, but epidemiological studies tend to suggest higher rates in those with earlier age of onset of type 1 diabetes. A fifth of patients with newly discovered type 2 diabetes have retinopathy at the time

of diagnosis while in type 1 diabetes, vision threatening retinopathy almost never occurs in the first five years after diagnosis or before puberty. However, after 15 years, virtually all patients with type 1 diabetes and two thirds of those with type 2 diabetes show evidence of background retinopathy and up to 75% of all people with diabetes will eventually develop retinopathy of some form. Therefore, the need for regular eye examination as a fundamental part of the routine care of all diabetic patients cannot be over emphasized.

Nephropathy

Diabetic involvement of the kidneys is referred to as diabetic nephropathy; and it is characterized by proteinuria $\geq$300 mg/24hours, increased blood pressure, and a progressive decline in renal function. At its most severe, diabetic nephropathy results in end stage renal disease requiring dialysis or transplantation, but in the early stages overt disease is preceded by a phase known as incipient nephropathy (or microalbuminuria), in which the urine contains trace quantities of protein (not detectable by traditional dipstick testing). Microalbuminuria is defined as urinary albumin excretion rate of 20-300 mg/24 hours or 20-200 µg/min in a timed collection.

The rate of decline in glomerular filtration rate varies widely between individuals. Fortunately, antihypertensive treatment especially with angiotensin converting enzyme (ACE) inhibitors even in normotensive patients slows the decline in renal function and improves survival among patients with diabetic nephropathy.

Diabetic Foot

The term "Diabetic foot" describes a multifaceted clinical problem both in aetiology and manifestations. Presentation is quite variable from foot ulceration to foot gangrene requiring amputation. Factors important in the pathogenesis of this complication are sensory neuropathy, angiopathy, infections, trauma and poor wound healing.

The "Diabetic foot" occurs globally with wide geographical variation. About 15% of people with diabetes have a foot ulcer during their life, in developed countries the annual incidence of foot ulceration is about 2-8% among the diabetic population, 85% of diabetes related amputations are preceded by a foot ulcer, 15% of

patients with diabetic foot ulcer may end up with an amputation. In developing countries, diabetic foot ulcers are unfortunately very common. This is often as a result of ignorance, poverty, bare foot walking, poor hygiene and most importantly feet not being examined by health care workers to detect the at risk foot and provide appropriate advice. In Zaria, diabetic foot sepsis is a major challenge and the commonest cause of hospitalization among diabetic patients. A retrospective review of case records of all patients admitted with diabetes foot sepsis at our hospital from January to December 2013, during which there was a cumulative strike period of 3 months by various health workers, a total of 142 diabetic patients were hospitalized during the period under review. Of this 44 (31%) of the patients were hospitalized as a result of diabetic foot sepsis. The age range of those who presented with diabetic foot sepsis was 32-75 years old. There was a male preponderance with 27 (61%) males and 17(39%) females. The right foot was affected in 21(48%) patients, the left foot was affected in 19(43%) while 4(9%) had bilateral involvement. Most of the patients presented with advanced disease, only seven (16%) had grade 2 disease, 14(32%) presented with grade 3 disease, 19(43%) presented with grade 4 disease while four (9%) presented with grade 5 disease. Five (11%) had below knee amputation while three (7%) died during hospitalization. It was concluded that diabetic foot sepsis is an important health problem in our environment there is need to identify those at risk early enough to prevent this potentially debilitating complication[40].

Pathogenesis of the Diabetic foot

The pathogenesis of events that could end up with a lower limb amputation or gangrene usually starts with the formation of a foot ulcer (break in the continuity of the skin). This is almost always preceded by impairment of or complete loss of sensation as a result of neuropathy. Sensory neuropathy results in failure to appreciate noxious stimuli such as pain, extremes of temperature and pressure, thermal, physical or mechanical trauma could go on unnoticed leading to ulceration. Ulceration in the diabetic foot could be complicated by super added bacterial infections; poor blood supply as a result of macro-angiopathy could impair healing as would oedema from local inflammation or autonomic neuropathy. Sensory

neuropathy should be actively sought for at each clinic visit; and patients with sensory neuropathy as well as other high-risk features need advice on foot care to minimize the risk of ulceration. To prevent diabetic foot complications, the diabetic is advised:

- Not to walk barefoot (always wear shoes.)
- Keep feet clean and moist (just as your face.)
- Use shoes that must give room for toes to move freely.
- Not to use hot water bottle on the foot.
- Never to remove corns or calluses personally.
- To examine feet daily.

Musculoskeletal Complications

Diabetes quite commonly affects the musculoskeletal system, resulting in significant morbidity. Several mechanisms may contribute to skeletal damage, including increased urinary excretion coupled with lower intestinal absorption of calcium, as well as the alteration of vitamin D regulation. Decreased or increased insulin and IGF-1 concentrations and the effects of the accumulation of glycation end products on bone tissue may also play a role. A possible genetic predisposition is also currently under investigation. As far as bone mass is concerned, in adult patients with type 1 diabetes a moderately reduced bone mineral density has been shown in both axial and appendicular skeleton. On the contrary, patients with type 2 diabetes seem to have higher bone mineral density in respect to healthy control subjects, especially when overweight women are considered. These manifestations may go undiagnosed or simply overlooked in daily clinical practice. However, symptoms may be severe and incapacitating. Fortunately, many of these complications are amenable to treatment with resultant improvements in the quality of life; it is therefore essential for patients and clinicians to be aware of the possible musculoskeletal complications of diabetes. The various musculoskeletal complications of diabetes mellitus are:

- Diabetic cheiroarthropathy.
- Flexor tenosynovitis.
- Dupuytren's contracture.
- Carpal tunnel syndrome.
- Frozen shoulder.
- Calcific periarthritis.
- Reflex sympathetic dystrophy.
- Diabetic osteoarthropathy.

- ***Diffuse idiopathic skeletal hyperostosis.***
- ***Muscle infarction.***

The Metabolic syndrome

Vice Chancellor Sir, distinguished audience. The changes in life style of our society characterized by excessive caloric intake and decreased physical activity does not only result in obesity and diabetes. It also results into a much more serious medical problem referred to as the metabolic or the insulin resistance syndrome. This is constellation of disorders such as hyperinsulinaemia, insulin resistance in the aetiology, central obesity, glucose intolerance, systemic hypertension, ischaemic heart disease, and peripheral vascular disease. Reaven in 1988[47], coined the term 'Syndrome X' to refer to the clustering of these conditions, and suggested insulin resistance as the underlying cause, and the resultant hyperinsulinaemia as being responsible for the components of the syndrome. This cluster, among other terminologies, is also referred to as the 'metabolic syndrome'. There is evidence to suggest that the prevalence and expressivity of this syndrome varies from one population to another and even within populations.

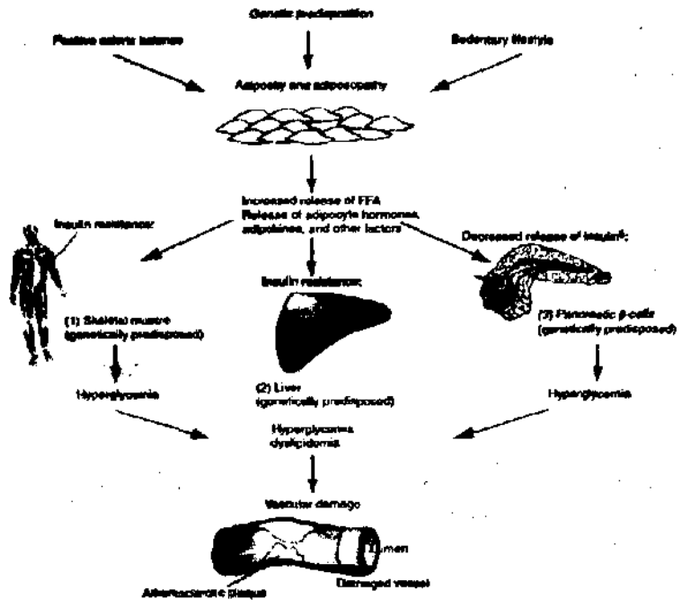


Figure 5: depicts the metabolic syndrome

The World Health Organization (WHO) has suggested a working definition of this syndrome in individuals with glucose intolerance, i.e. glucose intolerance with any two or more of: insulin resistance, arterial hypertension, central obesity or a body mass index (BMI) >30 kgM^2, dyslipidaemia, and microalbuminuria. Using this definition, we studied the prevalence of this syndrome among diabetics in Zaria.[11] Type 2 diabetic patients had higher waist: hip ratios (WHR) and body mass indices (BMI) compared to control subjects ($p<0.05$ and $p<0.01$ respectively). Components of the Metabolic Syndrome were common among type 2 diabetic Nigerians. Insulin resistance and central obesity were the most common, respectively occurring in 40% and 95% of type 2 diabetic Nigerians while hypertension occurred in 32%. There was a positive but statistically non-significant correlation between the various components of the syndrome. It is concluded that the Metabolic Syndrome is common among type 2 diabetic Nigerians. Table 1 and table 2 below shows the different components of the syndrome among the study population. Of particular note is the higher rate of obesity when defined using WHR implying that central obesity is more prevalent than when obesity is defined by calculating BMI. It is noteworthy that Vague[44] as early as 1947 has demonstrated that central obesity is much more injurious to health than peripheral obesity.

Table : components of the Metabolic Syndrome among type-2 diabetic in Zaria.

	Males	Females	Total	p value
Metabolic syndrome	10 (36%)	6 (50%)	16 (40%)	NS
Central obesity	26 (93%)	12 (100%)	38 (95%)	NS
Hypertension	7(25%)	6(50%)	13 (32%)	<0.05
Insulin resistance	10 (36%)	6 (50%)	16 (40%)	<0.05
BMI ≥30 Kgm^2	0 (0%)	2 (17%)	2 (5%)	<0.05

Central obesity = WHR >0.85 for females and >0.9 for males.
Insulin resistance = HOMA IR value >2.0.

Table : indices of obesity among diabetic and control subjects.

Anthropometric index	Type 2 diabetic patients			Control subjects			p value
	Males Number (%)	Females Number (%)	Total Number (%)	Males Number (%)	Females Number (%)	M...	
BMI (kg/m...							
WHR							...01

Management of Diabetes

The aim of therapy in diabetes is to improve the quality of life, achieve and maintain normoglycaemia, prevent hypoglycaemia and most importantly prevent acute and chronic complications of diabetes. The DCCT trial has conclusively shown that it is possible to achieve these objectives to a large extent[41]. To achieve these, life-style modification with or without some form of pharmacological (drug) intervention would be required. Non-drug modalities of therapy especially ***physical exercise*** and ***dietary modification*** have been recognized by physicians as far back as 600 BC to be beneficial in the management of diabetes. In the same vein, ***diabetic education*** is the corner stone of any successful management program, and is probably the most important tool to achieve optimal diabetic control. ***Diabetic education*** is therefore as important as any form of intervention[45,46]. Globally, there is no dissenting voice that diabetes education is a strong factor in achieving, and sustaining good glycaemic control; preventing diabetic complications and improving the quality of life for the diabetic individual[18].

Physical Exercise

Physical exercise is known to reverse insulin resistance and promote normal glucose homeostasis. Physical activity guidelines from the American Diabetes Association and the American College of Sports Medicine have suggested that intermittent moderate-intensity exercise is beneficial and can improve the health status of individuals with impaired glucose tolerance and diabetes[47]. Specifically, the guidelines recommend the accumulation of 30 minutes of moderate-intensity physical activity per day, and have

classified brisk walking (3–4 miles per hour), gardening, and general home-care activities as moderate-intensity exercise. It is important to stress that exercise does not necessarily mean a specific organized program such as playing tennis, weight lifting, jogging or using some form of equipment such as a treadmill. However, simply moving the body as in walking to places of worship, shopping or visiting relatives on foot provides as much health benefits as organized programs provided that the shorter bouts of physical activity add up to at least 30 minutes a day. In addition to improving insulin sensitivity, exercise could also help in a weight reducing program in overweight diabetic subjects' thereby further improving insulin sensitivity and glycaemic control. The following are *benefits of exercise:*

i. Improves insulin sensitivity.
ii. Helps in weight-reduction.
iii. Reduces plasma glucose levels.
iv. Relieves stress.
v. Helps to reduce high blood pressure.
vi. ↑HDL cholesterol, ↓LDL and Total cholesterol
vii. Reduces risk of stroke & heart attacks.
viii. Results in general feeling of well being

Dietary Management

Diet has long been recognized to play significant roles in the aetiology and sustenance of several illnesses. This is more so in diabetes[46], where dietary changes have been shown to play significant roles in its development. Dietary control inconcert with weight loss, and exercise would help reduce postprandial glycemia and assist in losing additional weight, as well as in optimizing risk management for macro-vascular disease, a common complication of the disorder[48,49].

There has been a significant change in the dietary advice given to diabetic individuals from what used to be preached. In the past, low-carbohydrate diets were widely publicized, and unfortunately, many patients and care providers are still holding on the erroneous notion that diabetics should take little or no carbohydrates. However, recent evidence and expert recommendations suggest that diets with severely restricted

carbohydrate content are not recommended for patients with diabetes. Such diets are fraught with the dangers of ketosis that may adversely affect renal function. Secondly and most importantly, patients who take insulin or oral tablets are at increased risk of hypoglycemia with low or no carbohydrate content meals. Furthermore, such diets often contain excessive amounts of protein, fat or both with attendant risks of cardiovascular and renal morbidity respectively. However, within the context of a balanced diet, individual food choices may have dramatic effects on blood glucose levels. Therefore, the key is to effective nutritional therapy in diabetes is individualization[49] .

Strictly speaking there are two forms of dietary intervention in diabetes: these are a measured diet and the unmeasured diet, the latter is what is practiced in our environment. In the measured dietary intervention, the amounts of calories to be taken daily are calculated and the source of that energy distributed among the major food classes (carbohydrates, protein and fat). In the unmeasured diabetic dietary intervention on the other hand, different foods are classified in to three categories those to be taken without restrictions such as vegetables, those to be taken in moderation this includes complex carbohydrates, protein and vegetable fat; and those to be out rightly avoided such as simple sugar containing foods such as candies, honey, cakes etc. This is the commonest form of advice given in most developing countries where it is not practicable to measure how much calories are being consumed at each meal. This has brought the concept of the Diabetes Food Pyramid (figure 6), which has six sections for food groups that vary in size. The largest group made up of grains, beans, and starchy vegetables are placed on the bottom of the pyramid. This implies that more of grains, beans, and starchy vegetables should be eaten compared to any of the other foods. The smallest group is placed at the top of the pyramid and consists of fats, sweets, and alcohol. This implies that very little or not at all from this group should be eaten. The general advice given to diabetics is:

- Eat a variety of foods.
- Balance food intake with physical activity
- Emphasize on grain products, vegetables, and fruits.
- Emphasize on diets low in total fat content.
- Advise a diet moderate in sugars.
- Reduce sodium intake.
- Increase potassium intake.

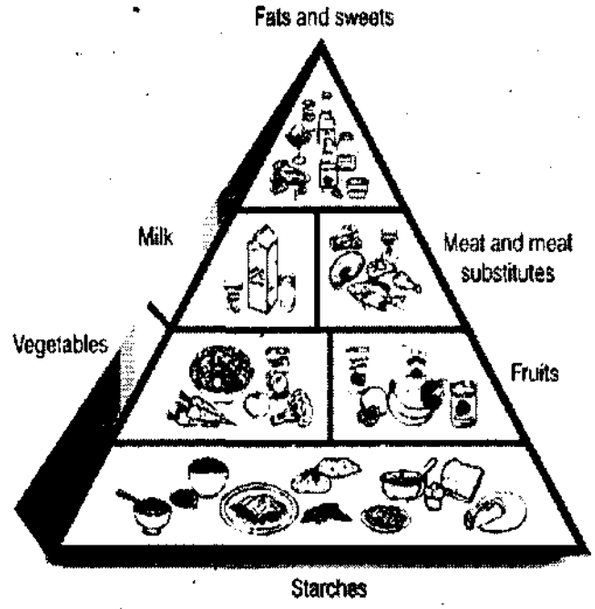


Figure 6: The Diabetic Food Pyramid

Variety is an essential component

Eating a wide variety of foods, even from the same food group should be emphasized. This helps to ensure that all required nutrients are ingested. For example: Within the fruit group, bananas are good sources of potassium while oranges are a good source of vitamin C.

Carbohydrate Intake

It is acceptable for the carbohydrate to be at a higher level provided that the food eaten is rich in soluble fiber and have a low *glycaemic index (GI). The* GI is a concept developed to rank foods based on the increase in blood glucose levels after the ingestion of 50 grams of carbohydrate from a test food, compared to a standard amount of 50 grams of white Bread. In other words, the GI of a particular food is defined as the area under the glucose response curve for that food compared with a standard control) the standard control is usually glucose or white bread.

The GI depends largely on the rate of digestion and rapidity of absorption of carbohydrate, the faster the rate of digestion and absorption, the higher the GI. It is possible to increase the amount of carbohydrate intake by increasing the intake of foods high in soluble fiber (legumes, lentils, some fruits, oats and barley) without adverse glycaemic consequences. Emphasis should therefore be placed on grain products, vegetables, and fruits. Carbohydrates such as grains, dried peas, beans, lentils; parboiled rice and many other staple foods of traditional cultures have low glycaemic indices and should be encouraged. It is advisable to eat grains, which should preferably be unpolished as polishing reduces the fiber content leading to higher glycaemic indices. These foods provide the least concentrated sources of calories and should provide the mainstay of the diet.

Immediately after eating a high glycemic index meal, serum levels of glucose, insulin, and incretin hormones increase dramatically. Within two to four hours following such a meal, blood glucose levels fall, leading to counterregulatory hormone release and increased free fatty acid release. The glucose excursion that follows a low vs high glycemic index meal directly affects postprandial glycemia. For example, the change in plasma glucose following ingestion of 50 g of spaghetti which has a GI of 41 is 50% of that seen following the ingestion of the same quantity of white bread which has a GI of 70 an hour after the meal. High glycaemic index foods such as soft drinks, ice cream and cookies provide large quantities of calories with little or no nutrients and should be avoided especially when weight reduction is intended.

Glycaemic load

Although central to the choice of food, the GI of food is not the only factor considered. Also considered is the glycaemic load (GL), which has been developed taking into cognizance both the quality and quantity of the carbohydrates consumed. Each unit of dietary GL represents the equivalent glycaemic effect of 1 g of carbohydrate from white bread, which is used as the reference food. High GL values are exhibited by such foods as low-amylose white rice, baked potatoes and corn flakes breakfast cereal. Some foods such as carrots and watermelon have high GI but low GL values. Since their GL are low these foods provide only a small amount of carbohydrate and hence could be ingested.

Protein Intake

The current guidelines recommend eating between 10% and 20% of required calories as protein. This is based on the fact that diabetics have similar protein requirements as the general population. Although the recommended daily allowance (RDA) for protein is 0.8 grams per kilogram of body weight; reducing protein intake to 0.6 g per Kg body weight per day could reduce albuminuria and improve renal hemodynamics in type I diabetes patients with incipient and established nephropathy. Such diets do not worsen blood glucose levels and do not lead to protein under nutrition. Suggestions that high-protein diets contributes to the pathogenesis of early diabetic nephropathy would be a very strong reason against high protein diets among people with diabetes in general. This is at variance to the old teaching where diabetics were advised on high protein diets. Furthermore, the preferred protein source is of plant rather than animal origin to reduce total fat and cholesterol intake. Vegetable proteins are generally less bioavailable, and may allow more overall intake in those with early nephropathy.

Sugars and Sweeteners

Ranges of non-nutritive sweeteners such as saccharin, aspartame etc. are available for diabetics and may be useful if added to drinks and cooking. Though aspartame is a dipeptide, it is intensely sweet and very little quantities are required to make food and drinks palatable. All these sweeteners provide useful means of reducing energy intake.

Vitamins and Minerals

Micronutrients have at one time or the other been the subject of interest in diabetes; however, there is no solid evidence that those with diabetes have different requirements for vitamins and minerals than those who do not have diabetes. Nevertheless, because of the increased frequency of hypertension and cardiovascular risks in diabetes, diabetic patients should be advised to restrict sodium intake to 6 grams per day or less, and in the setting of hypertension 3 grams per day. Similarly, increased potassium intake and sometimes-additional supplementation is particularly important when indicated, as this micronutrient has been shown to consistently lower blood pressure in population studies.

Though epidemiological evidence exists about the protective effects of antioxidant nutrients such as carotenoids, vitamin C, flavenoids, and tocopherols against coronary heart disease in non-diabetic individuals, recent evidence has shown conclusively that

supplementation with antioxidant nutrients such as vitamin E, vitamin C, and ß-carotene has no impact on cardio vascular outcomes and hence cannot be recommended routinely for diabetic patients. Rather, the emphasis should be on good glycaemic control; and control of the other well established risk factors such as obesity, dyslipidaemia, cessation of smoking, control of blood pressures etc.

Diabetes Mellitus in the Nigerian African

Vice Chancellor Sir, Fellow academics, distinguished guests. Diabetes mellitus presents a significant public health challenge in developing countries of Sub-Saharan Africa and Nigeria is no exception. Our community currently faces a double disease burden represented by increased rates of non-communicable diseases such as diabetes and hypertension; as well as endemic and emergent infections such as malaria, diarrheal diseases, tuberculosis, and HIV/AIDS.

In a survey of diabetes mellitus in Giwa and Makarfi local government areas of Kaduna state in 1996, we screened a total of 317 people aged 15-75 years. Diabetes occurred in five of the volunteers (1.6%) [50]. A few years later our colleagues from the Department of Community Medicine found a prevalence of 2.0% in Dakace village about 10 km from Zaria[51]. Equally more worrisome is the high prevalence of pre diabetes in the general population especially women[52]; suggesting that they have started the journey to become diabetic if remedial measures are not taken. In fact about 316 million people worldwide (6.9% of adults) were estimated to have IGT in 2013.[7] The vast majority (70%) of these people live in low- and middle-income countries, with the highest burden of IGT found among the Southeast Asian and European population with prevalence rates of 13.2% and 10.2% respectively while Africa was estimated to have a prevalence of 7.3%. By 2030, the number of people with IGT is projected to increase to 471 million (8.0% of the adult population) [7].

The increase in the number of people suffering from diabetes is linked to unhealthy ways of living and lifestyle such as consumption of excess calories, usually refined sugars in the form of soft drinks and snacks; and reduction in the level of physical activities with the consequent development of obesity and insulin resistance. Indeed the rampant consumption of soft drinks in our communities is obvious to all and sundry and often time's people are oblivious of the fact that large amounts of calories are ingested with every sip of these drinks. We have studied the sugar and caloric contents of the common soft drinks consumed in Zaria[53], and found

that they indeed contain high levels of calories. The result of excess caloric consumption coupled with a sedentary life style is obesity.

Obesity, type 2 diabetes mellitus, and their associated long-term complications are emerging as critical, worldwide public health problems. The cause of obesity in developing countries has been attributed to the current lifestyle, where urbanization, better economic development and an increase in income have resulted in diet changes referred to as nutritional transition[54], and less physical activity. In our community study we found that 13.1% of the subjects had obesity, while overweight was recorded in 18.5% (i.e. 36. % of the population had higher than normal BMI) of study participants[55].

Diabetes in the Nigerian African is characterized by predominance of type-2 diabetes as in the rest of the world, high prevalence of complications and poor blood glucose control. For example, a multicenter study across seven tertiary health centers in Nigeria[56] in which a total of 531 patients made up of 209 (39.4%) males and 322 (60.6%) females were enrolled, made the following findings. The mean age of the patients was 57.1 ± 12.3 years with the mean duration of diabetes of 8.8 ± 6.6 years. Majority (95.4%) had type 2 diabetes mellitus while 4.6% had type 1 diabetes. The mean FPG, 2-HrPP glucose, and glycated haemoglobin (HbA1c) were 8.1 ± 3.9 mmol/L, 10.6 ± 4.6 mmol/L, and 8.3 ± 2.2%, respectively. Only 32.4% and 20.4% patients achieved the ADA and IDF glycaemic targets, respectively. Most patients (72.8%) did not practice self-monitoring of blood glucose. Hypertension was found in 60.9%. Diabetic complications found were peripheral neuropathy in 59.2%, retinopathy 35.5%, cataracts 25.2%), cerebrovascular disease 4.7%, diabetic foot ulcers 16.0%, and nephropathy 3.2%. It was concluded that most Nigerian diabetics have suboptimal glycaemic control, are hypertensive, and have chronic complications of diabetes. This is similar to our findings in a ten year prospective collation of all cases of diabetes mellitus seen at our hospital, over a 10 year period[57]. Type-2 diabetes mellitus was the commonest form of the disorders encountered, chronic complications of diabetes mellitus were common, the commonest being peripheral neuropathy in 44% of cases, systemic hypertension in 25% of cases and diabetic foot gangrene in 2.8% cases.

There is a striking rarity of coronary artery disease among Nigerian diabetics despite poor control, and the presence of other risk factors such as hypertension and dyslipidaemia[58, 59]. This observation is perhaps as a result of the relative hypoinsulinaemia[60-63] and relative rarity of insulin resistance among our patients [2, 64].

Furthermore, the platelets of our diabetic patients are known to disaggregate even after aggregation.[65]

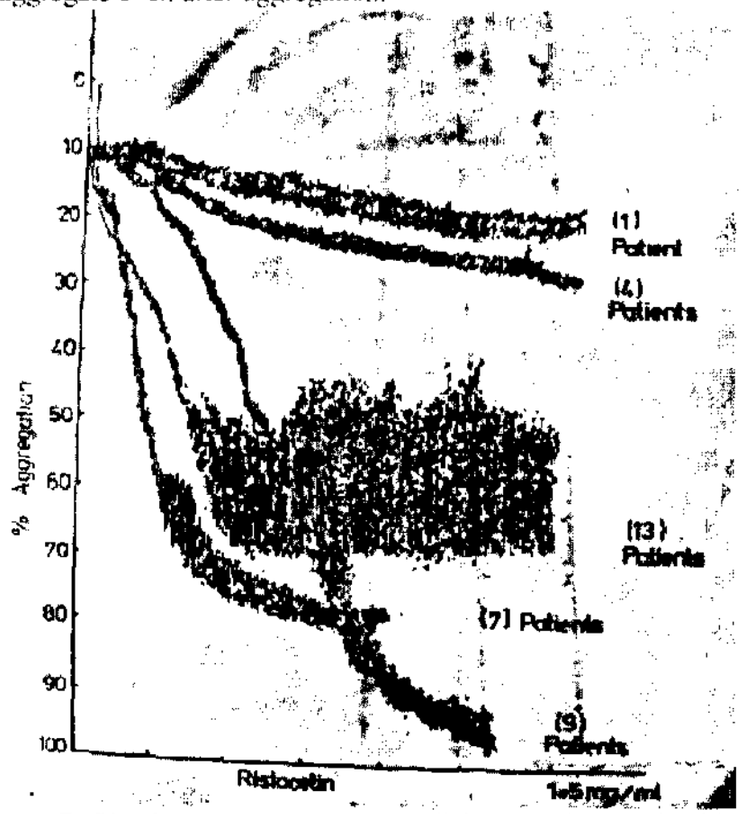


Figure 7: Platelet aggregation among diabetic and control subjects in Zaria

Challenges of managing diabetes mellitus in Nigeria

Managing diabetes in our environment is often challenging both for the patient, his family and indeed the health care provider as a result poverty, ignorance and poor health seeking behavior and inaccessibility of quality health care. Poverty, ignorance and poor health seeking behavior results in late presentation and is a possible reason why majority of our patients present with complications[56, 57, 66]. The impact of poverty, ignorance and poor health seeking behavior manifest more in diabetic children than adult diabetics, as it is possible that some, if not a significant majority of the affected

children succumbed to the illness at home out of parental ignorance and high cost of orthodox medical care. It is a daily routine in our hospitals for patients or their guardians to sign against medical advice and return home due to financial reasons, and or to seek alternative therapy or spiritual help[67].

Use of alternative and complementary therapy

Most of the time, the patients visit the local traditional healers before coming to the hospital [68-70]. Traditional medicine or complementary and / or alternative medicine (CAM) refers to health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to treat, diagnose and prevent illness or maintain well being[71].

The frequency of utilization of CAM is increasing worldwide and is well documented in both African and global populations to be between 20 to 80%[72]. Multiple therapy practices involving combined use of CAM particularly herbal medicines and prescription medications is prevalent in our population[69, 70]. Many herbal remedies have not undergone careful scientific assessment and some have the potential to cause serious toxic effects and major drug-to-drug interactions. Cultural and economic reasons are largely responsible for use of CAM. These include failure of modern medicine to cure the underlying problem and the perception that CAM is cheaper than conventional medicine. In countries like Nigeria, possible reasons for the use of CAM include the strong advertisement by alternative practitioners that CAM is a panacea to all diseases thus encouraging patients to try them. Another possible explanation is the cultural beliefs of Africans that illnesses have a spiritual origin. Patients are thus interested in finding an explanation for their symptoms or the root cause of their problems and therefore consult with alternative practitioners. In Nigeria, the use of herbal remedies which is perceived to be cheaper, is on the increase due to the poor economic state and the increasing costs of orthodox medicines as well as cultural reasons. Furthermore, the advertising strategies on the media and especially using vehicles with megaphone from one neighborhood to another, which do not inform but persuade customers, have also made the use more popular. Although several CAM practices and herbal remedies are promising

for diabetes treatment, further scientific studies are needed in order to establish safety, efficacy, drug-drug interactions and mechanism of actions of the herbs being used[72]. We studied the anti-diabetic potential of certain plant extracts in diabetic rats [73-75], and found them to have the potential of lowering blood glucose levels. Obviously further studies need to be done on these extracts. Furthermore, one of our PhD students is planning to study the effect of *moringa olifera on* the Pharmacokinetic Parameters of Metformin Hydrochloride in our Diabetic Patients. This would obviously throw more light on this subject in due course.

Prevention and Control of Diabetes Mellitus

Technically speaking, the prevention and control of diabetes mellitus could be discussed at three levels. These are primary prevention, secondary prevention and tertiary prevention.

Vice Chancellor Sir, distinguished audience it would not be out of place to start with the following quotation by A quote of Musa Ibn Maymun the Influential Andalusian Jewish physician and philosopher (March 30, 1135 Córdoba- December 13, 1204 Fostat, Egypt). Which is ***"Live sensibly- among a thousand people, only one dies a natural death, the rest succumb to irrational modes of living"***

Primary prevention

At this level, activities are geared towards reducing the incidence of diabetes in the community by the identification and appropriate management of known modifiable risk factors. This is cost effective in economic terms, as a slight change in the prevalence of these factors leads to significant changes in the prevalence of diabetes, which translates, into colossal sums of money saved. The known modifiable risk factors for all forms of diabetes are specifically targeted. Obviously, the strategy for the control of type1 diabetes would differ from that of type 2 diabetes; which would also differ from the strategy for the control of secondary diabetes.

Control of Type 2 Diabetes

As previously noted, type 2 diabetes mellitus is the commonest form of diabetes. Unfortunately, majority of diabetics

remain undiagnosed and even among those diagnosed, diabetes is often diagnosed relatively late in the course of the disease, at a point when many patients have already developed complications[7]. In addition, management is lifelong and challenging for both patients and physicians. Therefore, even slight changes in the incidence and prevalence of this form of diabetes would translate to significant changes in the overall incidence and prevalence of diabetes. Fortunately, major advances have been made in our understanding of the prevention of type 2 diabetes. Interventions that can reverse glucose intolerance early in its course may be the key to primary prevention of the long-term complications of diabetes[7, 11, 12, 71]. Clinical trials have convincingly shown that lifestyle modification is the most effective tool in the prevention or delay of type 2 diabetes[76]. For overweight and obese patients, a modest weight-loss goal of 5–10% (often < 20 lb) can substantially reduce the risk of diabetes. Moderate-intensity physical activity such as brisk walking for at least 150 minutes per week also plays an important role in reducing diabetes risk, even in the absence of weight loss. For patients who are unable to achieve these lifestyle goals or those who progress despite exercising and losing weight, metformin has also been proven effective, especially in younger obese patients. Acarbose, when tolerated at the maximum effective dose, may also confer a moderate risk reduction. Data regarding thiazolidinediones are conflicting, and the reports of cardiovascular and fracture risk make this option less attractive as a prevention strategy. However, none of these medications are as robust in diabetes prevention as the lifestyle intervention strategies, and cost-effectiveness analyses suggest that pharmacotherapy may have greater financial costs. Prevention of diabetes is our most powerful intervention, and successful implementation of these proven strategies should be the main focus. One of the earliest studies conducted in a Chinese community involving 577 men and women with impaired glucose tolerance were randomized to a program of diet, exercise, or both. Dietary intervention focused on increased amounts of vegetables and reduced consumption of alcohol and simple sugars: overweight individuals (those with a BMI > 25 kg/m2) were encouraged to lose weight[11]. The exercise group was instructed to increase their daily activity by the equivalent of 20 minutes of moderate activity, such as brisk walking, and the diet-plus-exercise group was asked to do

both exercise and dietary modification. After 6 years of follow-up, all three interventions were similarly effective, with risk reductions of 31–46% compared to an untreated control group. Similarly, the Finnish Diabetes Prevention Study (DPS) [77] randomized 522 overweight (average BMI 31 kg/m2) middle-aged individuals to either intensive lifestyle modification or a control group. Life style modification entailed both specific dietary recommendations and exercise guidelines with a weight-loss goal of 5% of total body weight; and at least 30 minutes of combined aerobic activity and resistance training daily. This study demonstrated a clinically significant impact of intensive lifestyle changes in the reduction of diabetes. At the 3-year follow-up, the group reduced their cumulative risk by 58% compared to the control subjects. During the first year, the intervention group lost an average of 4.2 kg, which appeared to be the primary mediator of diabetes risk reduction. Further analysis demonstrated the impact of exercise on the risk reduction of diabetes: moderate to vigorous activity of at least 2.5 hours per week reduced the incidence of diabetes by 63–69%. In the extended follow-up (3 years after the active intervention was completed), the intensive lifestyle group maintained a 36% relative reduction in diabetes incidence, suggesting that these benefits could be maintained outside of a structured clinical trial setting.[71]

Similarly, the Diabetes Prevention Program (DPP) [12], the largest study on lifestyle intervention for the prevention of diabetes to date randomized 3,234 overweight participants with impaired glucose tolerance and elevated fasting glucose in the United States to one of three interventions: intensive lifestyle intervention (ILS), metformin, or placebo. The ILS group was instructed to follow a low-calorie, low-fat diet, with a weight-loss target of 7% of baseline body weight and an exercise goal of at least 150 minutes per week of moderate-intensity physical activity. The ILS group participated in a 16-week core curriculum focused on behavior modification, diet, and exercise education during the first 24 weeks, followed by at least monthly reinforcement. After an average follow-up of 2.8 years, the ILS group achieved a mean weight loss of 7%, and three-fourths of the participants met the exercise targets during the first 6 months of the study. The ILS group had a 58% reduction in the development of diabetes compared to the placebo group. Weight loss was the predominant predictor of reduced diabetes incidence,

with a 16% reduction of developing diabetes for each kilogram of weight lost. However, participants who did not achieve their weight-loss targets but were able to achieve the exercise goal also benefited (44% risk reduction compared to placebo). The effectiveness of the ILS intervention was similar in men and women and among racial and ethnic groups. Recommendations for life style modification are summarized in table 3 below.

Table 3: recommended life style modifications[76]

1. Moderate level physical activity such as brisk walking for at least 30 minutes per day, 5 days per week.
2. Weight loss of 5-15% of starting weight with 1-2lb weekly.
3. Limit fat intake to <30% of daily caloric intake.
4. Reduce portion sizes and daily caloric intake.
5. Increase intake of fruits, vegetables and fibre in diet.

Secondary prevention

Results of the DCCT studies have important implications for preventing diabetes complications in people with diabetes mellitus. The DCCT study compared the effects of standard control of blood glucose versus intensive control on the complications of diabetes. Intensive control meant keeping HBA1C levels as close as possible to the normal value of 6 percent or less. The study concluded that intensive control significantly reduces the rates of chronic complications meaning complications of diabetes are to a large extent preventable by appropriately controlling blood sugars. Specifically, eye disease 76% reduced risk, kidney disease 50% reduced risk and neuropathy 60% reduced risk.

Since up to half of people with type 2 diabetes have vascular complications at the time of diagnosis and since the development of chronic diabetic complications is a function of the duration and severity of hyperglycaemia, early detection of diabetes is therefore essential. Several international recommendations from authoritative bodies support screening for type 2 diabetes as the benefits of early diagnosis in asymptomatic individuals will outweigh any harm associated with screening, early diagnosis, or the side effects of early therapy[7]. Screening (by way of measuring fasting blood glucose levels) should be considered for high risk patients, especially those who are middle aged and obese, have a history of gestational

diabetes, or have a family history of diabetes. These are summarized in table 4 below.

Table 4: recommendations for screening for Diabetes and Prediabetes[76]

1. Screening should be considered in all adults that are overweight(BMI>25kg/m^2) and have the following additional risk factors: ❖ Physical inactivity. ❖ First degree relative with diabetes. ❖ Women who deliver large babies (birth weight >3.5kg) or were diagnosed to have GDM. ❖ Hypertension. ❖ HDL cholesterol <35mg/dl or triglyceride >250mg/dl. ❖ HbA1C >5.7%, IGT or IFG on previous testing. ❖ Other conditions associated with insulin resistance such as polycystic ovary disease, acanthosis nigricans, severe obesity e.t.c. 2. In the absence of the above criteria, screening should begin at age 40-45 years. 3. If results are normal, repeat screening at least at 3-yearly intervals with more frequent testing if indicated.

Recommendations

Vice Chancellor Sir, distinguished audience, it is obvious that we are today facing an epidemic of diabetes as a result of drastic changes in our lifestyles from that bequeathed to us by our forefathers. The need to retrace our steps cannot be overemphasized. There is the urgent need for concerted efforts by governments, communities and educational institutions to key into preventive measures to curb this epidemic that if left unchecked could paralyze economic and social development of our society. The following measures would certainly help to reduce the menace if implemented:

i. Vigorous public enlightenment campaigns on the need to as much as possible avoid refined and fatty foods and encourage the consumption of boiled foods instead to reduce total caloric intake and reduce the risk of obesity in the community. Public enlightenment is also necessary on the need for the community to consume grains such as corn,

sorghum and millet unpolished, as polishing reduces the fibre content and increases the glycaemic index of the grains.

ii. Regulatory authorities must put in place measures to encourage active life style in the community and schools. The ministry of education should as a matter of policy insist that to be licensed, a school must have adequate space and provision for recreation by pupils and at least 30 minutes per day must be provided for in the time table for sports.

iii. Governments at all levels, pharmaceutical companies, communities and non-governmental organizations (NGO) such as the Diabetes Association of Nigeria (DAN) should put in measures to periodically and at regular intervals, put in place all necessary measures to screen the population at risk of diabetes and prediabetes to ensure early diagnosis and management.

iv. There is need to train and retrain middle level and specialist manpower to properly identify and manage diabetes to reduce the prevalence of both acute and chronic complications of diabetes.

v. Diabetic medications especially insulin are life saving drugs and should be seen and treated as such. There is therefore the urgent need to make them both accessible and affordable for all that require them. Government, NGO and philanthropic individuals would do well if at least insulin could be made available and free for all insulin requiring diabetics.

vi. The University should as a matter of urgency consider the setting up of a diabetes institute with the sole mandate of training middle level and senior manpower for our health system as well as research into the peculiarities and opportunities that exist in our traditions and culture that could tame the diabetic epidemic. The International Diabetes Federation (IDF) and the WHO would be willing partners and funders for such an institute.

The Vice Chancellor Sir, distinguished guests, thank you for your kind attention and may God Almighty save us from the evil of gluttony.

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