Diabetes Mellitus in Africans

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The first report of the WHO Expert Committee on Diabetes Mellitus, made in 1965, contained a classification of patients based on age of recognised onset[1]. Since then, different pathogenic mechanisms leading to diabetes mellitus with different courses and prognosis have been revealed[2], which have led to reviews of this classification. An interim classification, based on that of the Diabetes Data Group of the National Institutes of Health, USA[3] has recently been recommended in the second report of the WHO Expert Committee on Diabetes Mellitus[4]. A simplified version is shown in Table 1.

Table 1. Classification of diabetes mellitus and other categories of glucose intolerance.

A. Clinical Classes
(i) Diabetes Mellitus
— Insulin-Dependent—Type 1
— Non-Insulin-Dependent—Type 2
(a) non-obese
(b) obese
— Other types associated with certain conditions and syndromes such as pancreatic disease, hormonal diseases, drug or chemical induced conditions, insulin receptor's abnormalities, etc.
(ii) Impaired Glucose Tolerance
(a) non-obese
(b) obese
(c) associated with certain conditions and syndromes.
(iii) Gestational Diabetes
B. Statistical Risk Classes
Normal glucose tolerance but with increased risk of developing diabetes

Diabetes mellitus is no longer considered to be a single disease entity but rather a state of chronic hyperglycaemia which may result from many environmental and genetic factors, often acting together. It is therefore not surprising that diabetes mellitus may show some geographical and ethnic variations. However, it has been difficult to delineate what these variations are, particularly in developing areas of the world such as Africa, where epidemiological information may be lacking or inadequate. Despite this, it has been possible to identify certain types or sub-types of diabetes that are peculiar to the tropics, Africa included. It is therefore important, when classifying diabetes in the African along WHO lines, to point out any differences or difficulties which may be encountered. Only by doing this in different geographical or ethnic groups will the relevance or irrelevance of the global application of the new WHO classification be appreciated.

Insulin-Dependent Type—Type 1

This is a well-recognised entity, particularly in Caucasians of the developed countries in whom the diabetes often has (a) an onset which is typically abrupt, (b) particular HLA tissue types, (c) circulating islet cell antibodies (ICA) early in its course, and (d) a family history of diabetes or autoimmune diseases. The difficulties of characterising this type of diabetes mellitus in Africans are obvious.

HLA tissue type studies have not been extensive in Africa. However, since different environmental and genetic factors operate in different races and ethnic groups, it would not be surprising if the HLA linkage patterns also differed. In fact, young negroes of South Africa have higher frequencies of BW35[5].

Only minimal work has been done on ICA in African diabetics. Table 2 shows the autoantibody status of 68

Table 2. Characteristics of the 68 Nigerian diabetics in whom autoantibodies were studied.

Age group (years)	30 recent onset diabetic subjects			38 diabetic subjects with symptoms over 6 months' duration		
	M	F	Total	M	F	Total
Under 40	12	7	19	6	8	14
	(4)*	(4)	(8)	(1)	(4)	(5)
Over 40	8	3	11	13	11	24
	(2)	(1)	(3)	(2)	(1)	(3)
Total	20	10	30	19	19	38
	(6)	(5)	(11)	(3)	(5)	(8)

*Figures in parentheses denote patients on insulin

Nigerian diabetics[6]. ICA measured at the time of diagnosis was found in only two diabetics (a male aged 20 on insulin and a male aged 41 years on tablets) out of the 30 newly diagnosed cases, 11 of whom were insulin treated. This study shows that ICA are probably rare in young Nigerian diabetics, treated with or without insulin, compared to Caucasian diabetics. Irvine *et al.*[7] found ICA in 65 per cent of newly diagnosed Caucasian diabetics who were on insulin compared to 11.1 per cent in this

Table 3. Autoantibodies in 68 Nigerian diabetics and 68 age and sex matched non-diabetic controls.

Autoantibodies	Cases No. (%)	Controls No. (%)
Pancreas		
Islet cell	4 (5.9)	1 (1.5)
Glucagon cell	0	1 (1.5)
Somatostatin cell	0	0
Thyroid		
Thyroglobulin	1	0
Microsomal	1	0
Stomach		
Gastric parietal cell	2 (2.9)	1 (1.5)
Intrinsic factor	0	0
Adrenal cytoplasmic	0	0
Anti-nuclear	6 (8.8)	6 (8.8)
Smooth muscle	0	0
Mitochondrial	0	0
At least one of the above	14 (20.5)	9 (13.2)

study. In our study (Table 3), no diabetic with ICA had other autoantibodies, in contrast to the findings in insulin-dependent Caucasian diabetics[8]. This rarity of autoantibodies may be due to an altered immunological state produced by many parasitic infections which are common in Africa[9]. Two of our patients over 40 years old who were not insulin-dependent had ICA, unlike the Caucasians, in whom all the milder forms of diabetes (Type 2) are not associated with ICA at any stage of the disease. From the study, there is an indication that the division of diabetes into Type 1 and Type 2 on the basis of ICA and insulin dependence may not generally fit the pattern of diabetes as seen in Nigeria and possibly other parts of Africa.

The family history of diabetes is often difficult to obtain from diabetics in the developing countries because of social discrimination; in addition, autoimmune disorders are thought to be rare in Nigeria and possibly in other parts of the tropics[10]. It thus appears that the typical insulin-dependent type of diabetes, as seen in Caucasians, is not very common in Africa. Indeed, it is recognised that diabetes in children and adolescents (who form the bulk of Type 1 diabetics) is rare in tropical countries as a whole[11]. The genetic susceptibility to insulin-dependent diabetes probably differs among races. It is also possible that environmental factors account for some of these interpopulation differences. Such factors may include timing, dosage or frequency of exposure to certain viruses, and the nutritional status. In developing African countries, juvenile diabetics with acute onset of the disease often die in ketosis, undiagnosed and in the absence of good medical facilities. An accurate census of diabetes in the young is therefore difficult.

Non-Insulin-Dependent Type—Type 2

The diabetics in this group are divisible into non-obese and obese.

It appears that the majority of diabetics seen in Africa belong to this major class, often independent of the age of onset. Typical non-insulin-dependent diabetes has a gradual onset, usually occurs in late middle age, is not associated with any HLA type, and is often discovered by chance. The greatest risk factors appear to be obesity and physical inactivity. In Caucasians many of the diabetics in this group are obese, often with family aggregation of diabetes and obesity; but in Africa the role of obesity in this type of diabetes is in doubt. Osuntokun *et al.*[12] found that most of the adult-onset diabetics at Ibadan were not overweight. We had a similar finding at Enugu[13]. In the Bantus, obesity does not play much of a role as a diabetogenic factor[5]. One must admit that most of the studies relating to obesity and diabetes in Africans were done with figures for Caucasians. To my knowledge no such figures are widely available for Africans.

In tropical African countries, many non-insulin dependent diabetics do not have a gradual onset of their disease. They often present abruptly with heavy glucosuria, often needing insulin treatment for initial control of symptoms and hyperglycaemia but subsequently being dependent on oral drugs and/or diet[14]. Some even remit when no longer obese[15]. In addition, many young black Africans tend to have a mild diabetes similar to the 'maturity onset diabetes of the young' found rarely in Caucasians.

Diabetes Mellitus associated with Certain Conditions and Syndromes

The spectrum of conditions and syndromes found is wide and may vary from one population to another. In Africa, the following conditions are clearly important: calcific fibrosis of the pancreas, malnutrition, alcohol, and widespread infections. Pancreatic diabetes is probably commoner in Africa in the younger age group than elsewhere.

Pancreatic Diabetes (calcific fibrosis of pancreas: juvenile tropical pancreatitis syndrome)

A syndrome of pancreatic insufficiency occurring in young people in the tropics and characterised by abdominal pain, diabetes (mostly insulin-dependent), malabsorption and pancreatic calcification was first noticed in Indonesia in 1959 by Zuidema[16]. Since then, the condition has been reported in the following African countries: Ghana, Malawi, Nigeria, Uganda, Zaire and Zambia. The aetiology of this syndrome is speculative. Zuidema attributed the condition to malnutrition. An association between pancreatic damage and consumption of tapioca (cassava) has been widely cited[17].

Table 4 shows the major clinical features in 30 patients with this syndrome seen at the Teaching Hospital, Enugu, from 1973 to 1979[18]. The histological characteristics of this disease are dilatation and obstruction of the main duct and ductules of the pancreas; the ducts often contain inspissated mucus or laminated secretions undergoing calcification, and some other ducts contain calculi[19,20]. Infiltration by lymphocytes and plasma cells occurs and narrowing of part of the main duct, described in some Asian cases[21], is not obvious in African cases. The hypothesis put forward by Nwokolo and Oli[18] is

Table 4. Major clinical features in 30 patients with juvenile tropical pancreatitis syndrome at Enugu (1973–1979).

Clinical feature	No. of patients (%)	Onset of symptom or sign
Abdominal pain	26 (86.7)	17 patients (57%) before age 10 years
Diabetes	26 (86.7)	19 patients (64%) before age 10 years
Steatorrhoea	10 (33)	Uncertain
Pancreatic calcification	30 (100)	Uncertain

that plugs (inspissated mucus or laminated secretions) are the result of pancreatic stasis due to prolonged lack of food in the stomach and/or gastroenteritis and dehydration. Most plugs are probably dislodged during convalescence when protein-containing foods are eaten and stimulate a vigorous flow of pancreatic juice. The sluggish pancreatic flow produced by very low protein diets may not dislodge plugs. Repeated infection and anorexia can enlarge the plugs, which ultimately calcify. This hypothesis, more than any other, explains the high incidence of the syndrome in the lower social class, its geographical distribution in the tropics where infections are common; its onset in childhood, and the pathological findings in the pancreas. The question of why only a few of those exposed to similar environmental stresses get this syndrome must be raised. An HLA study has not been performed on these patients to rule out genetic selection.

Malnutrition

Widespread protein malnutrition is common in Africa. In protein malnutrition there seems to be a low insulin output in response to glucose challenge indicating either a reduction in the number of B cells or the functional impairment of these cells. Whether continued protein deprivation would ultimately result in irreparable damage to B cells or increase their susceptibility to harmful environmental factors needs further study, as does the role of malnutrition in the aetiology, course and prognosis of diabetes in Africa. The J type of diabetes may be classified as belonging to this group.

J (for Jamaica) diabetes. In 1955 Hugh Jones[22] described 13 thin young Jamaican diabetics whose disease required therapy with high doses of insulin and who did not readily become ketotic even after stopping insulin. He called this J-type or Jamaican diabetes. This type of diabetes has been described in the following African countries: Ghana, Kenya, Malawi, Nigeria, South Africa, Uganda, Tanzania and Zaire. However, follow-up of Hugh Jones's original patients showed that many had become prone to ketosis and that their high insulin requirements were due to dietary excess[23]. The features described by Hugh Jones were (a) low age of onset, (b) leanness, (c) high insulin dose, and (d) relative resistance to ketosis. It is, however, not clear if this type of diabetes is a peculiar manifestation of ordinary childhood-onset diabetes or if it is aetiologically different. The cases reported nearly all had a history of severe malnutrition in childhood. Whether J-type diabetes actually exists is debatable. There are many reasons why I am sceptical about its existence. (1) The follow-up of Hugh Jones's original cases by Tulloch and MacIntosh[23] showed them to be prone to ketosis. (2) Jamaican immigrants in England have been found to have diabetes similar to that of the indigenous population[24]. (3) Ahuja *et al.*[25] found that two-thirds of young Indian diabetics, who were thought to be ketosis-resistant, became ketotic after their insulin was stopped. (4) Campbell[26] found that patients who seemed at first to have J-type diabetes were not really insulin-dependent and could be treated with oral hypoglycaemic drugs. Perhaps these patients with J-diabetes are the tropical equivalent of maturity-onset diabetes of the young, as suggested by Jarrett[27].

The calcific fibrosis of the pancreas may also be classified as belonging to the malnutrition group, as it is found in a background of protein malnutrition in the early years of life.

Alcohol

Some alcoholic drinks taken in certain areas of South Africa contain large quantities of iron which may damage the pancreas and cause diabetes[28]. Excessive intake of alcohol may also lead to chronic pancreatitis and diabetes. In the coloured ethnic group of South Africa, calcific pancreatitis is almost always alcoholic in origin and almost all patients are overtly diabetic[5].

Infections

The enterovirus Coxsackie B4, rubella and mumps have been implicated as causal factors of diabetes in man[29]. The infections are thought to cause diabetes in those having HLA-related susceptibility. The only documented virus infection associated with diabetes in Africa is viral hepatitis. Oli and Nwokolo[30] described 11 patients who developed diabetes after an attack of infectious hepatitis during the Eastern Nigerian epidemic of 1970-72 after the Nigerian Civil War. The report thus confirmed that the pancreas is sometimes permanently damaged during infectious hepatitis. In contrast to the virus-induced diabetes in Caucasians, most of the reported cases in Nigeria were not insulin-dependent. Virus infections abound in Africa and further evidence is needed to show the relationship between virus infection and diabetes and also between genetic susceptibility and virus infection.

The role of certain native herbs in causing diabetes mellitus, possibly by damaging the pancreas, has to be remembered. Dodu[14] thought they might be responsible for certain forms of temporary diabetes mellitus seen in the tropics.

Impaired Glucose Tolerance Test

Impaired glucose tolerance is found in Africa, as elsewhere. The new criteria for the diagnosis of impaired glucose tolerance[4] will allow more meaningful comparisons to be made. However, they may be confounded by

the fact that Africans tend to have lower fasting blood glucose than Caucasians[31].

Gestational Diabetes

This is defined as diabetes that develops during pregnancy but remits after delivery. A true incidence in most tropical countries is almost impossible to determine, but gestational diabetes is encountered in Africa.

Statistical Risk Classes

As in other countries, people with normal glucose tolerance but with an increased risk of developing diabetes exist in African countries.

In conclusion, the prevalence and types of diabetes vary greatly among countries and populations. Although the prevalence is thought to be lower in the developing countries such as those of Africa, it appears that the disease is becoming increasingly common as the standard of living improves. Although I find the new WHO classification generally satisfactory in the African context, it appears that the bulk of African diabetics belong to the non-insulin-dependent Type 2 group; that the typical insulin-dependent Type 1 diabetes is rare in Africans; that genetic and immunological factors play a smaller role in causation of diabetes in Africans; and that environmental factors such as malnutrition, alcohol, and widespread infections are clearly more important in the causation of diabetic syndromes in Africa.

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