GLOBAL EPIDEMIC OF TYPE 2 DIABETES: IMPLICATIONS FOR DEVELOPING COUNTRIES

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INTRODUCTION

Diabetes has reached epidemic proportions in many populations. Current estimates suggest that the number of persons with diabetes will reach 250 million by 2010 and 300 million by 2025. The majority of these patients will have type 2 diabetes and reside in developing countries. Type 2 diabetes and its associated long-term complications continue to accelerate among patients who reside in developing countries. Apart from microscopic complications, cardiovascular disease, with its attending morbidity and mortality, is on the rise in the developing countries. Current evidence suggests that environmental factors are major determinants of the increasing rates of diabetes. Addressing these environmental factors offers a unique opportunity for preventing diabetes; health programs that aim to encourage physical activity and discourage (or limit) overweight and obesity deserve significant attention. Prevention must be the cornerstone for international health organizations and ministries of health in developing countries as they plan diabetes management programs. (Ethn Dis. 2003;13(suppl2):S2-102–S2-106)

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PREVALENCE OF TYPE 2 DIABETES IN DEVELOPING COUNTRIES

Type 2 diabetes is a genetic disease with strong familial and environmental components.15–19 While prevalence rates of the disease are increasing everywhere, some countries are experiencing an epidemic of type 2 diabetes.1–4 Black Africans living in rural and urban regions of Africa are no exception. The prevalence rates of diabetes range from 0.5%–2.5% in rural areas, to 4%–6% in urban areas. Several recent studies have found remarkable increases in the prevalence rates of type 2 diabetes in most developing countries, such that 90% of patients with diabetes exhibit type 2.4,6,11 The increasing prevalence of type 2 diabetes in developing countries can be partly ascribed to modernization, and partly to the adoption of a Western lifestyle, with its associated risk factors, such as calorie-dense diets, less physical activity, and obesity. These are modifiable risk factors that can be implemented to prevent, or slow, the rate of increase in type 2 diabetes in these developing regions.

BETA CELL DYSFUNCTION IN IMPAIRED GLUCOSE TOLERANCE AND TYPE 2 DIABETES IN DEVELOPING COUNTRIES

Several studies have examined the beta cell secretion in persons of African
The prevalence rates of type 2 diabetes, and its associated long-term complications, continue to increase among populations of developing countries. Therefore, cardiovascular disease associated with diabetes will continue to account for a significant percentage of the morbidity and mortality in developing countries.

Ancestry who exhibit impaired glucose tolerance (IGT), and type 2 diabetes. Similar to other populations, such as African Americans in the Western world,1-3 Black Africans having IGT and type 2 diabetes manifest blunted acute first insulin secretion to intravenous glucose tolerance test as the earliest beta cell lesion.20-31 Mbanya et al30 reported that a significant proportion of the offspring of Cameroonian persons with type 2 diabetes had either type 2 diabetes (4%), or impaired glucose tolerance (8.5%). Similarly, we found that the acute first phase insulin responses to intravenous glucose were moderately blunted in the Ghanaian patients with IGT,21 similar to responses exhibited by African-American patients with IGT and type 2 diabetes. Further, Shires et al30 demonstrated that Black Africans living in South Africa have lower serum c-peptide levels, compared to Europeans and Indians.30 Because most of these studies were cross-sectional, the sequential changes in beta cell function could not be assessed in the Black African patients. Results from the limited number of longitudinal studies of beta cell function in sub-Saharan African (SSA) patients, such as that conducted by Joffe et al,28 demonstrate more rapid deterioration of beta cell functioning in the progression of IGT to type 2 diabetes in Black South Africans, as compared to White South Africans. In summary, these studies demonstrate that: 1) the severity of beta cell secretory dysfunction varies considerably in Black Africans; and 2) moderate-to-severe beta cell dysfunction is a paramount pathogenetic feature of IGT and type 2 diabetes, respectively, in patients in the sub-Saharan African region.

**Potential Factors Affecting Beta Cell Function in Type 2 Patients with Diabetes in Developing Countries**

The reasons for the inconsistencies of reports on serum insulin and/or c-peptide responses in diverse Black SSA populations, residing in different geographical locations, are uncertain. However, several possibilities can be entertained. First, there may be differences in the impact of obesity and body fat distribution, and, possibly, of lifestyle, physical activity, and fitness, on in vivo insulin sensitivity. Lifestyle factors may be modulated or influenced by the degree of urbanization and Westernization within the country. Second, people of African ancestry may be heterogeneous, both genetically and phenotypically. Third, several studies have demonstrated that the major determinants of insulin secretion include genetic inheritance, race/ethnicity, and the prevailing insulin sensitivity. Fourth, the prevalence and incidence rates of IGT and type 2 diabetes parallel the degree of obesity in various ethnic and racial populations. In a study from Finland, Vaag et al18 reported significant inter-individual insulin secretion variations in identical twins discordant for type 2 diabetes. To the best of our knowledge, no similar data exist on concordance/disCORDANCE for type 2 diabetes among identical Black twins. Nevertheless, our results demonstrate that after adjusting for obesity, the rates of insulin secretion (insulin and c-peptides), and hepatic insulin extraction, were similar in Blacks, regardless of country of origin.21,22 This finding led to speculation that Black African subjects could be genetically predisposed to accelerated apoptosis with rapid deterioration of beta cell functioning, especially in the presence of metabolic stressors. Fifth, the beta cell dysfunction in Black sub-Saharan Africans could be a consequence of an intraterine (in utero) fetal life during pregnancy. These fetuses experience generalized growth retardation (ie, being small for their gestational ages), which predisposes them to future beta cell dysfunction, insulin resistance, and cardiovascular diseases (Barker and Hales Hypothesis). Similarly, it is possible that early childhood malnutrition results in beta cell dysfunction during adulthood. In support of this hypothesis, Crowther et al32 demonstrated that 152 7-year-old children, originally of low birth weight, exhibited rapid post-natal weight gain, higher plasma insulin at 30 and 90 minutes, and higher serum glucose responses at 30 minutes during OGTT, when compared to children who were normal-weight babies.

Several potential environmental beta cell cytotoxic agents could play a role in the etiology of type 2 diabetes in Black African regions. Cassava has been suspected of being such an agent; however, recent studies have questioned the validity of the findings on cassava’s causal effect on beta cell dysfunction in SSA, due to methodological problems in the original studies.23 Nevertheless, it is possible that a defective nutritional environment, acting in conjunction with chronic exposure to environmental toxins, such as cassava, alcohol, childhood infections (eg, bacterial, parasitic, malaria, and viral) or antimalarial agents, could play a role.
Insulin resistance (IR) is the hallmark of type 2 diabetes in the Western world, and is genetic and familial, with an acquired component. IR is found predominantly in the skeletal muscle, adipose tissue, and hepatic tissues, in several populations, and precedes the development of IGT and type 2 diabetes by decades. Indeed, IR is found in subjects without diabetes but having hypertension and obesity, as well as in subjects with parents with type 2 diabetes. It is now clear that race and ethnicity, independent of family history of type 2 diabetes, also determine insulin resistance in several populations. Recent studies have demonstrated that insulin resistance is associated with obesity in a given population. The consequences of insulin resistance are progressive deterioration in the rate of glucose disappearance or dispersal in the peripheral tissues, and, perhaps, beta cell exhaustion. The latter, whether genetically inherited (eg, apoptosis) or not, could precipitate the development of IGT and type 2 diabetes, in individuals susceptible to the disease. We have recently confirmed these findings in indigenous Ghanaian patients with IGT and type 2 diabetes, who reside in their native country. The reduced insulin sensitivity index was also observed in the first-degree relatives without diabetes of our native Ghanaian patients with type 2 diabetes. This is consistent with the earlier findings of Ezenwaka et al among first-degree relatives of Nigerian patients with type 2 diabetes. Thus, insulin resistance is a concomitant condition of type 2 diabetes patients of sub-Saharan regions, apparently preceding the development of clinical disease by decades.

**The Role of Insulin Resistance in the Pathogenesis of Type 2 Diabetes in Developing Countries**

In the Western, industrialized countries, the major determinants of insulin resistance, in addition to genetics, are obesity (BMI >30 kg/m² for both genders), or overweight (BMI >25 kg/m² for both genders), and sedentary lifestyles. It has, therefore, been suggested that in populations with lower prevalence rates of obesity, such as native Black Africans, the degree of insulin resistance is predominantly determined by genetic inheritance, and further affected by conventional risk factors, such as obesity, physical inactivity, etc. However, the emerging evidence indicates that, in developing countries, obesity, even a BMI between 25 kg/m² and 30 kg/m², is strongly associated with IGT and type 2 diabetes. As exhibited in Figure 1, slight increases in BMI, such as from 22 kg/m² to 25 kg/m², nearly doubled the prevalence of type 2 diabetes in the diverse populations of SSA origin, although they resided in different geographical locations, and exhibited varying rates of obesity.

The prevalence rate of obesity in SSA Blacks has been estimated at 10%–15%. This is remarkably lower than the prevalence rate of 50% in African Americans, residing in the United States, and 35% in Afro-Caribbeans residing in the UK. Similar to other populations, the prevalence rate of obesity in SSA patients with IGT and type 2 diabetes ranges from 40% to 60%. However, a remarkable number of SSA patients with IGT and type 2 diabetes are lean, or maintain a normal body weight, contrasting starkly to the 90% prevalence rate of obesity (BMI of 30 kg/m²) found in both African Americans, and Afro-Caribbeans who reside in the United Kingdom. As shown in Figure 1, several investigators have found a positive, and direct, relationship between the prevalence of obesity and type 2 diabetes in patients living in Iba-

**Obesity and Insulin Action in Developing Countries**

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**Potential Role of Environmental Factors in the Pathogenesis of Type 1 Diabetes and Type 2 Diabetes in Developing Countries**

**Geographical Location**

Papoz et al and others have indicated differences exist in the clinical presentation of type 2 diabetes in SSA. The patients with type 2 diabetes who are lean, often reside in rural areas, and the clinical picture is similar to that of patients with type 1 diabetes, as is the BMI, which is approximately 22 kg/m² for both non-obese patients with type 2 diabetes, and patients with type 1 diabetes. In addition, the beta cell functioning in the non-obese patients with type 2 diabetes is severely diminished during fasting, and during glucose challenge. As expected, the serum c-peptide levels were significantly lower in the lean, compared to the obese, patients with type 2 diabetes. In addition, the obese patients with type 2 diabetes often reside in cities, or urban areas, and Westernization, with its associated obesity and insulin resistance, tends to modify the metabolic characterization of type 2 diabetes in SSA.

**Subtypes of Diabetes in Developing Countries**

Undoubtedly, diabetes has a multivariate expression and presentation in developing countries, and subtypes of diabetes are found in developing countries, such as sub-Saharan Africa (SSA), sub-continental India, and Jamaica. Typically, the non-obese patients with type 2 diabetes in SSA regions could be described as insulin sensitive, or insulin resistant, variants in these populations, which creates confusion as to the distinction between patients with type 1 diabetes...
diabetes and non-obese patients with type 2 diabetes, who exhibit malnutrition-related diabetes mellitus (MRDM) at the time of initial presentation. The latter manifests as fibrocalcific pancreatitis with associated type 2 diabetes in patients younger than 30 years. These patients are extremely thin, with BMI <19 kg/m², blood sugars in excess of 18 mmol/L (350 mg/dL), have no ketonuria, despite elevated glucagon, and manifest high insulin need greater than 2 U/kg/d. Characteristically, these patients have a past history of severe childhood malnutrition, and exhibit radiological evidence of calcific pancreases.

**SUMMARY**

In summary, the global increase in the prevalence and incidence of type 2 diabetes has been particularly significant in developing countries in Africa, with a persistent rural to urban gradient. We believe the increase in prevalence of diabetes can be ascribed partly to more accurate determination of disease, and to adoption of a Western lifestyle. In Black African patients with type 2 diabetes, the pathogenetic hallmark of the disease is severe beta cell dysfunction, with variable degrees of insulin resistance. The insulin resistance appears to occur with obesity, although it may precede the development of glucose intolerance by decades. Understanding these etiopathogenetic factors for both diseases could enhance the development of effective preventive strategies, and/or management paradigms, for patients with type 2 diabetes residing in sub-Saharan Africa. Finally, the increasing prevalence and incidence rates of type 2 diabetes, in addition to the disease's short- and long-term complications, pose a growing threat to the economies of developing countries. In particular, cardiovascular diseases, which account for 75% of all deaths in patients with diabetes, will also continue to increase. The projections suggest increasing morbidity, greater loss of productive life years, and reduced life expectancy, in patients with diabetes in developing countries.

**CONCLUSIONS**

We conclude that the burden of health care in patients with diabetes residing in developing countries, especially those in Africa, will be enormous. Without carefully conceived health delivery systems, diabetes will continue to be a fatal disease in developing countries. Therefore, prudent measures (eg, mass media education) to prevent type 2 diabetes, its associated long-term complications, and cardiovascular diseases, should be among the primary healthcare efforts in the developing African countries. Population-based strategies that emphasize prevention of diabetes will be crucial. In addition, policy development to ensure effective primary health care for the entire populace of developing countries, will play an important role in preventing diabetes, and in encouraging compliance with treatment regimens.

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