Autosomal dominant pattern of inheritance in type 2 diabetes in Nigeria

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Abstract
We investigated 212 patients attending 3 diabetic clinics in Lagos, Nigeria, and recorded family history, age of onset of diabetes, and body mass index. Analysis of family pedigrees showed that 3% of sibships followed an autosomal dominant pattern of inheritance. The mean age of diabetes onset among the dominant group was 25 years and obesity was uncommon. This suggests that these patients may have Maturity Onset Diabetes of the Young (MODY).

Type 2 diabetes is common in certain clusters of families and ethnic populations. This implies that there is a strong genetic influence. There are two forms of type 2 diabetes, namely the polygenic (late-onset) and monogenic (early-onset) forms. The polygenic form is the most common and usually occurs in patients with no family history of type 2 diabetes. The monogenic form is called Maturity Onset Diabetes of the Young (MODY) and can result from mutations in any one of at least six different genes. Many researchers have not been able to clearly distinguish the MODY type from type 2 diabetes.

Based on the prevalence of the disease and monozygotic twin concordance rates, the heritability of type 2 diabetes has been estimated at 70–80%. This value indicates a risk for first-degree, second-degree, and third-degree relatives.

Type 2 diabetes is also often associated with obesity, but the MODY type of diabetic is usually not obese. In addition to obesity, increasing age and a sedentary lifestyle greatly increase the risk of type 2 diabetes. In the US, cases are being diagnosed around the age of puberty and as young as 10 years. In the Pima Indians, also, cases can be 15–19 years old and in the UK cases have been aged between 13 and 15 years.

Recently, it has been reported that about 5% of Nigerians over 18 years old have diabetes. Researchers in other countries have highlighted the association of an autosomal dominant pattern of inheritance with the MODY diabetes type.

We describe here a small number of patients with what appears to be an autosomal dominant pattern of inheritance of type 2 diabetes.

Patients and methods
Subjects were patients attending diabetes clinics in the Medical Centre, University of Lagos; Clinical Center, Nigerian Institute of Medical Research (NIMR); and the Lagos University Teaching Hospital (LUTH). Data recorded from patients included family history of diabetes, age of onset of diabetes, and body mass index (BMI). A family pedigree was drawn up for the evaluation of inheritance pattern. Two-hundred and twelve (212) patients were recruited for this study. Clinical characteristics were used to distinguish patients with MODY from those with type 2 diabetes, including a prominent family history in two or more generations, a young age at presentation and absence of obesity. Data were analysed using means and percentages.

Results
About 23% of men and 14% of women had a family history of diabetes. Pedigrees with five or more sibships in two or more generations were selected for analysis of inheritance pattern (see Figure 1). Twenty-nine (14%) pedigrees appeared to transmit diabetes from one generation to another, and 24% of those 29 pedigrees transmitted the disease to half or more sibs. Also, 45% transmitted diabetes through three generations, while 55% did through two generations. From the 212 patients, 3% (seven families) followed a Mendelian pattern of inheritance.

The mean age of onset among the autosomal dominant group was 25 years, and their mean BMI was 26.1 (14% obese with a BMI >39.0).

Discussion
According to Mendelian segregation, when one parent is affected, half of the offspring are expected to be affected. But because of the small sibship size in humans, sibships in which the proportion of affected individuals is not half are common.

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humans are usually small, some families showed express
disease in two generations only. This may be because
of lack of diagnostic failures, as there is a high level of
ignorance about type 2 diabetes.

The polygenic form of type 2 diabetes is common, but
the monogenic form which is an autosomal dominant
condition is less common. Less than 5% of all subjects in
this study followed the autosomal dominant pattern, a
figure supported by WHO data. Our report also confirm
that the MODY subtype is usually a dominant condition
with an age of onset before 25 years.

It is important, however, to note that the numbers of cases in our study
were small, and there was a wide variation in age. Larger and more detailed studies of patterns of diabetes inheri-
tance in Africa would be very valuable.