

High Prevalence of Maturity-onset Diabetes of the Young (MODY) Among Indians

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This article describes the high prevalence of maturity-onset diabetes in the young (MODY) in an Indian clinic population of diabetic patients. MODY appears to be more common among Indians than among Caucasians. Only 27% of MODY patients had definite autosomal-dominant inheritance. In 73% the mode of inheritance was not definite. Microvascular complications were common and macrovascular complications rare. The high prevalence of MODY in this diabetes clinic might suggest an ethnic variation in diabetes. *DIABETES CARE* 1985; 8:371-74.

Maturity-onset diabetes of the young (MODY) refers to a type of diabetes in which the patients develop diabetes at <25 yr of age and respond to sulfonylureas or diet for a minimum period of 2 yr.¹ It has been reported that other characteristics of MODY are the mild course of the disease, absence of late complications, and autosomal-dominant inheritance.²

Recently, considerable heterogeneity has been described in MODY with respect to insulin responses to a glucose load,³⁻⁶ as well as the prevalence of vascular complications. According to Tattersall, vascular complications are infrequent in MODY² while in Fajans' series they are not uncommon.⁵ Tattersall suggested that there could be subgroups of MODY such as autosomal-dominant MODY and sporadic MODY.⁷ There are only a few reports on the clinical profile of these subgroups. The autosomal-dominant MODY is less prone to vascular complications of diabetes according to Tattersall.⁷ However, Fajans and co-workers^{5,6} have shown that the occurrence of vascular complications might be similar to that seen in usual non-insulin-dependent diabetes (NIDDM). Information is inadequate on the prevalence of MODY, but it appears to be a rare entity in Caucasians.⁸

Diabetes in the tropics presents several interesting differences from that seen in western countries. These include a low prevalence of insulin-dependent diabetes (IDDM)⁹ and the presence of peculiar types of tropical diabetes such as J-type diabetes¹⁰ and tropical pancreatic diabetes.¹¹ Even among patients with NIDDM there are differences such as a low prevalence of obesity and reversal of the sex ratio.⁹

This article describes the high prevalence of MODY in an

Indian clinic population of diabetic patients, and the vascular complications in various subgroups of MODY.

MATERIALS AND METHODS

Of a total of 4560 consecutive diabetic patients seen from 1981 to 1983 at the Diabetes Research Centre, Madras, in southern India, 219 patients (4.8%) could be classified as MODY. The diagnosis of MODY was based on the revised criteria of Tattersall⁷ as follows: (1) the age at onset was <25 yr, (2) control of diabetes was possible for at least 5 yr without insulin, and (3) ketosis was absent at all times. Patients classified as MODY had fasting plasma C-peptide values ≥ 0.30 pmol/ml and postglucose-stimulated values ≥ 0.6 pmol/ml, which are the mean values for NIDDM patients at our center.¹² The diagnosis of diabetes was based on the criteria of the WHO expert committee on diabetes.¹¹

All patients had a detailed family history analysis, and a full pedigree chart was drawn. All patients had a complete physical examination including fundus examination by both direct and indirect ophthalmoscopy by an ophthalmologist. The criteria recommended by the WHO multinational study were used for diagnosis of microvascular and macrovascular complications of diabetes.^{14,15} For neuropathy, bilateral absence of ankle jerks was taken as the criterion. A diagnosis of nephropathy was made if the 24-h protein excretion exceeded 500 mg in the absence of urinary tract infection or severe hypertension.

The body mass index (BMI) of the patients was calculated according to the formula: weight (kg) divided by the square

TABLE 1
Clinical details of the MODY patients

Group of MODY	Number	M/F	Mean age at onset (yr \pm SD)	Mean duration of diabetes (yr \pm SD)	Mean PP plasma glucose (mg/dl \pm SD)	Mean HbA _{1c} (% \pm SD)
Definite autosomal-dominant inheritance	59 (27)	27/32	21 \pm 2	15 \pm 3.0	236 \pm 26	9.5 \pm 1.0
Possible autosomal-dominant inheritance	117 (53)	54/63	22 \pm 3	11 \pm 4.0	218 \pm 22	9.0 \pm 1.2
Nonhereditary type	43 (20)	19/24	22 \pm 3	14 \pm 8	228 \pm 20	9.8 \pm 1.3

Numbers in parentheses denote percentage.

of the height (m). Those with BMI ≥ 27 were considered to be obese. Those with BMI ≤ 19 were classified as lean and all others as having ideal body weight.

MODY patients were further classified into three subgroups based on the family history of diabetes and autosomal-dominant inheritance. The criteria for autosomal-dominant inheritance were those of Roberts.¹⁶

Plasma glucose was estimated by the ortho-toluidine method¹⁷ and glycosylated hemoglobin by a colorimetric method.¹⁸

RESULTS

The 219 MODY patients included 100 men and 119 women; 63% were of ideal body weight, 32% were obese, and 5% lean. One hundred ninety patients (87%) had never received insulin. In 29 (13%) patients, insulin was given at some time. These included 15 patients who were pregnant, 5 who had systemic infections, and 9 patients with secondary failure to sulfonylureas, which occurred after a mean duration of diabetes of 12.5 yr.

The 219 MODY patients belonged to 201 different families. Thus, only 18 patients in this series were siblings of MODY

from the same family. In every instance, where a relative had diabetes, the diabetes was of the NIDDM type. In several families there were many more MODY patients. The latter were not included in the study because they were not actually tested at our center.

Twenty-seven percent of MODY had definite autosomal-dominant inheritance. In 53%, the mode of inheritance was probably autosomal dominant. In 20% of patients, the diabetes was of nonhereditary type. Table 1 shows the clinical details of these three subgroups of MODY. The patients in the three subgroups had similar plasma glucose and HbA_{1c} values.

Table 2 shows the vascular complications in the three subgroups of MODY. As expected, in all three subgroups the prevalence of all complications is higher in those with a longer duration of diabetes. Microvascular complications occurred equally frequently in all three forms of MODY. Though the prevalence rates of retinopathy, nephropathy, and neuropathy were marginally lower in those MODY with definite autosomal-dominant inheritance, the differences were not statistically significant.

Macrovascular complications were infrequent in all three

TABLE 2
Percentage distribution of vascular complications in MODY

Complications	<15 yr duration			>15 yr duration		
	Definite autosomal-dominant MODY (N = 43)	Possible autosomal-dominant MODY (N = 82)	Nonhereditary MODY (N = 34)	Definite autosomal-dominant MODY (N = 16)	Possible autosomal-dominant MODY (N = 35)	Nonhereditary MODY (N = 9)
BDR	2*	11*	6*	25*	41*	44*
Proliferative retinopathy	2	2	3	6	6	11
Nephropathy	7	5	6	6	23	33
Neuropathy	2	12	6	31	49	55
IHD	0	4	0	6	14	0

BDR: background diabetic retinopathy; IHD: ischemic heart disease.

Difference between the three subgroups of MODY: not significant (Fischer's exact probability test).

*Percentage with complications.

subgroups of MODY. While ischemic heart disease was seen in a small percentage of MODY patients, peripheral vascular disease was not present in any patient in this series.

DISCUSSION

This study presents a large series of MODY patients in India. As this report includes probands from 201 families, it might make the clinical profile of MODY more representative. If most of the probands are drawn from a few large families, the pattern of complications might tend to be similar because of identical genetic and environmental factors.

Surprisingly, there are very few reports on the prevalence of MODY even in a clinic population.^{1-3,19} Asmal and co-workers,²⁰ using a higher age limit for MODY (onset at <35 yr), noted that 10% of the Indian NIDDM patients in South Africa had a known age at onset of <35 yr. The prevalence of MODY was, however, low in black and white races in South Africa. Using similar criteria, we found that 18.5% of our NIDDM patients have known age at onset <35 yr and in 50% it is at <45 yr (Mohan et al., unpublished observations). These figures suggest that NIDDM type diabetes occurs at a younger age group among Indian diabetic individuals than in other racial groups. Panzram and Adolph⁸ estimated the prevalence of MODY in the community from the German Democratic Republic. In that study, it was seen that MODY constituted 0.15% of all diabetic patients. We found that 4.8% of patients seen at our center had MODY, which is one of the highest figures reported so far.

The major limitations of our study are that it is clinic-based and the data are based entirely on family history. However, a large multicenter population-based survey for diabetes done in India also indicated that the onset of NIDDM is at a younger age in diabetic Indians.²¹

The higher prevalence of MODY among female subjects in this series is interesting because diabetes is more common among men in India and in other tropical countries.²² The explanation for this could be that MODY type diabetes is diagnosed at an early age in young women because of routine blood tests done during pregnancy. Though Tattersall pointed out the presence of various subgroups of MODY such as autosomal-dominant and sporadic MODY,⁷ there are few data on their clinical profile. We found that in 27% of MODY patients definite autosomal-dominant inheritance could be established. In another 53% of patients the mode of inheritance was possibly autosomal dominant, while in the remaining 20%, inheritance was uncertain. A major limitation of such a classification is that it is based on the accuracy of family histories. If all members of the family were actually tested by performing blood glucose estimations, the figures might have been different. However, in five families that were completely tested, none of the relatives of the proband had diabetes. Thus, sporadic occurrence of MODY, which was pointed out by Tattersall,⁷ also occurs in our patients. Even though the MODY patients with definite autosomal-dominant inheritance have slightly lower percentages of mi-

crovascular complications, the differences are not statistically significant. Even in this group, in those with >15 yr duration of diabetes, 25% had background and 6% proliferative retinopathy. These findings support the observations of Fajans⁵ that MODY are prone to develop microvascular complications like "usual" NIDDM diabetic patients. They are in disagreement with Tattersall's view that MODY patients with autosomal-dominant inheritance are unlikely to develop microvascular complications.⁷

Macrovascular complications were infrequent in all subgroups of MODY in this series. The low prevalence of ischemic heart disease could be related to the younger age of the patients. The absence of peripheral vascular disease is striking, but this is in agreement with the findings of Jialal in South African Indians.²³ This might represent an ethnic variation, since in Caucasian MODY, macrovascular complications including peripheral vascular disease have been shown to be common.⁵ This suggests that heterogeneity exists within MODY patients of different ethnic groups.

To summarize, the prevalence of MODY in a clinic population in India appears to be much higher than that reported previously in Caucasian races. Even though familial aggregation is strong, definite autosomal-dominant inheritance is present only in 27% of MODY patients in this study. Even in this form of MODY, microvascular complications do occur. The frequency of MODY among Indians noted in diabetes clinics in India and South Africa suggests ethnic variation in diabetes.

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