



Incidence of diabetes mellitus in parents and grandparents of diabetic children

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■ The prevalence of diabetes mellitus in fathers and paternal grandparents was compared with that in mothers and maternal grandparents of 123 diabetic and 103 nondiabetic children. Although there was no difference in the prevalence of diabetes in mothers and maternal grandparents of diabetic children (12 relatives) compared with those of nondiabetic children (eight relatives), there was a higher incidence of diabetes in the fathers and paternal grandparents of diabetic children (19 relatives) than in those of nondiabetic children (five relatives). These data suggest that the factors that influence development of diabetes are more likely transmitted through the father's family than through the mother's.

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NUMEROUS studies have been designed to unravel the genetic inheritance of diabetes mellitus.¹⁻⁴ It is increasingly apparent that some of the difficulty in establishing reliable figures for the inheritance pattern of diabetes is related to the heterogeneity of the disease. Recent classifications have sought to make groups more homogenous by classifying disease as noninsulin-dependent diabetes mellitus (NIDDM), insulin-dependent diabetes mellitus (IDDM), gestational diabetes, and other secondary types. Although these groups are not completely homogenous, this classification has enhanced our understanding of these disorders.

In 1984, Warram and coworkers⁵ reported that IDDM was more common in the offspring of diabetic men than diabetic women. Reanalysis of several previous studies

confirmed this observation.⁶⁻⁸ Our study was designed to compare the incidence of diabetes mellitus in the paternal relatives (father and paternal grandparents) with that in the maternal relatives (mother and maternal grandparents) of diabetic and nondiabetic children.

METHODS

The parents of 128 children who developed ketosis-prone diabetes by age 15 were contacted to determine the incidence of insulin-treated diabetes mellitus in their families. The 123 families who had information on both parents and grandparents were included in this analysis. The age of onset, the use of insulin, and complications of diabetes in the families also were noted, but information regarding whether the diabetic individual was ketosis prone could not be verified. The parents of 103 age-matched nondiabetic children from a general pediatric practice provided the data for the control group. The diabetic children were patients of the authors or were interviewed at a summer camp for diabetic children. Informed consent was obtained from the parents of each

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TABLE 1
INCIDENCE OF IDDM DIAGNOSED BY AGE 40 IN PARENTS OF
DIABETIC AND NONDIABETIC CHILDREN

Parents of	Mother (%)	Father (%)	Total
Diabetics	3 (2.4)	5 (4.1)	123
Nondiabetics	1 (1.0)	0	103

child who participated in the study. Likewise, the prevalence in the mother and maternal grandparents and then the father and paternal grandparents of the diabetic and nondiabetic children was compared using chi square analysis.

RESULTS

Twenty-three percent of the diabetic children had a parent or grandparent with insulin-treated diabetes mellitus, whereas only 11% of the nondiabetic children had an insulin-treated parent or grandparent ($P < .02$). Ten percent of the diabetic children had a parent or grandparent who had the disease develop before age 40, whereas only 4% of the nondiabetic children had a parent or grandparent with insulin-treated diabetes diagnosed by age 40.

The incidence of insulin-treated diabetes in parents of diabetic and nondiabetic children is shown in Table 1. Overall, the incidence of diabetes was 2.4% in the mothers and 4.1% in the fathers of the diabetic children.

The prevalence of diabetes in the mother or maternal grandparents and father or paternal grandparents is shown in Table 2. There was no difference in the prevalence of diabetes in mothers and maternal grandparents of diabetic compared with nondiabetic children. How-

ever, there was a higher prevalence of diabetes in the fathers and paternal grandparents of diabetic children than in those of nondiabetic children ($P < .02$).

DISCUSSION

Genetic factors are considered important in the etiology of diabetes mellitus, but the exact mode of inheritance remains unclear. There is increasing evidence that diabetes mellitus is not a single disease but a heterogeneous group of disorders. Even classifying the disease into the two major categories IDDM and NIDDM has not completely eliminated the confusion regarding inheritance patterns. For example, several independent studies have shown that NIDDM may influence the inheritance of both NIDDM and IDDM.^{1,2} Therefore, it is likely that there is some overlap between these groups, even though there are different genetic forms of diabetes. Until there are markers for the different types of diabetes, only rough predictions for the risk of diabetes in close relatives of those whose disease is categorized as IDDM and NIDDM can be made.

The incidence of diabetes mellitus among parents of individuals with IDDM is reported to be from 2.6% to as high as 11%. The disorder occurs in 2.5–3% of mothers compared with 3.3–6.1% of fathers.³ In our study, 2.4% of mothers and 4.1% of fathers were insulin-treated by age 40.

Interestingly, there was no difference in the incidence of diabetes in mothers and maternal grandparents of diabetic children compared with those of nondiabetic children. However, diabetes occurred in 15% of fathers or paternal grandparents of diabetic children compared with a prevalence of 4% of fathers or paternal grandparents of nondiabetic children. Therefore, even when grandparents are considered, there appears to be a higher

TABLE 2
INCIDENCE OF IDDM IN PARENTS AND GRANDPARENTS OF DIABETIC (N=123) AND NONDIABETIC (N=103) CHILDREN

Relative	Of diabetics		Of nondiabetics	
	Total	Onset before 40	Total	Onset before 40
Mother or maternal grandparents	12	4	8	3
Father or paternal grandparents	19	8	5	2
Parents or grandparents*	28	12	11	4

* In several families, diabetes was present in both maternal and paternal parents and/or grandparents.

prevalence of IDDM in the father's family compared with the mother's.

This suggests that the factors that influence development of diabetes are more likely transmitted through the father's family than through the mother's. The reason for this differential transmission of IDDM from diabetic fathers is not known. It may be related to a lower frequency of recombination between linked alleles during gametogenesis in men than in women.^{9,10} If diabetes is a result of a combination of several alleles, a specific combination is more likely to be received intact from an affected father than from an affected mother.

Another possibility is that diabetic women may have increased fetal loss of potentially diabetic children. This could involve either metabolic or immunologic mechanisms that result in failure of implantation and/or abortion. Although all these studies do not clarify the mode

of inheritance of diabetes, these results should affect genetic counseling of diabetic patients who are concerned about the development of diabetes in their relatives.

We conclude that parents and grandparents of diabetic children more often have insulin-treated diabetes mellitus than the parents and grandparents of nondiabetic children. Although the reason is not clear, the disease is much more prevalent in the father and paternal grandparents of diabetic children than in the mother and maternal grandparents.

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