Original Research Paper

Age at diagnosis and family history in Type II diabetes: implications for office screening

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Key Points

- In this study, 40 per cent of patients with Type II diabetes had a first degree relative with diabetes
- Patients with a positive family history were diagnosed four to seven years earlier than patients with no family history of diabetes
- This association holds true for the three major ethnic groups of Chinese, Malays and Indians in Singapore
- There was no difference in age at diagnosis between male and female patients
- Family physicians should screen for diabetes earlier among asymptomatic subjects who have a positive family history of diabetes

ABSTRACT

Background: Type II diabetes is aheterogenous disease, the mode of inheritance of which is not yet clear. A large proportion of patients have a positive family history of diabetes. This paper examines the association between family history and age at diagnosis in patients with Type II diabetes.

Methods: A cross-sectional study was undertaken, involving 972 patients with established Type II diabetes on follow-up at a primary care clinic. Demographic and clinical data were obtained from direct interview and case records. Statistical analysis of patient subgroups was done by appropriate tests of significance.

Results: Patients with a positive family history were diagnosed at an earlier age of between four to seven years compared to patients with no family history. The relationship holds true for each of the three major ethnic groups represented in the study population. There was no gender difference in the age at diagnosis.

Conclusions: Family history is an independent predictor of age at diagnosis in patients with Type II diabetes.

INTRODUCTION

Type II (non-insulin-dependent) diabetes mellitus is a common chronic problem in ambulatory care: the majority of these patients are followed up by family physicians. It is a heterogenous disease with both polygenic inheritance and environmental factors contributing to its clinical expression. A high proportion of patients with Type II diabetes

have relatives who also have diabetes. In recent population studies, positive family history in diabetic subjects was reported to be as high as 60 per cent in rural Mexico[1] and 63 per cent in Kuwait.[2]

It is well known that relatives of diabetic subjects are at a higher risk of developing diabetes compared with those who have no such family history. In the Australian Diabetes Screening Study, the risk ratio of diabetes for those with a positive family history was 1.7;[3] while among three Alaskan Eskimo populations, the odds ratio of diabetes, after adjustment for age, was 4.4 in those with a family history of diabetes.[4]

Type II diabetes has a long subclinical phase, and its onset probably occurs at least 12 years before clinical diagnosis.[5] As a result of this, diabetic complications are already present at the time of diagnosis, eg, from several studies, between 10 and 29 per cent of newly diagnosed patients were found to have retinopathy.[5] Screening therefore becomes important in the early detection of Type II diabetes, so treatment can be instituted early and the development of complications can be reduced or delayed.

Thus, does having a positive family history alert an individual towards his/her higher risk status? Is diabetes diagnosed earlier in those with a positive family history? This paper aims to examine the influence of positive family history on the age of diagnosis in patients with Type II diabetes, and other demographic factors that may affect this association.

METHODS

The study population consisted of 977 consecutive patients with Type II diabetes on follow-up at a primary care clinic in Singapore. This is a government-subsidised general outpatient clinic which caters mainly to residents of the surrounding housing estate. The services provided include preventative care such as immunisation, treatment for acute illness, as well as follow-up care for patients with chronic illness such as diabetes and hypertension.

Patient selection criteria for the study included documented diagnosis of Type II diabetes as noted in the case records, and being on the diabetic register maintained by the clinic. Newly diagnosed patients were included, as were Type II diabetic patients who had secondary drug failure and were currently on insulin therapy. Patients who were on insulin since

TABLE 1: DESCRIPTIVE PROFILE OF STUDY SUBJECTS (N=972)

Profile		Number (%)
Age in years	Mean	61.1
	Standard deviation	10.7
	Range	28-87
Gender	Male	483 (49.7)
	Female	489 (50.3)
Ethnic Group	Chinese	789 (81.2)
	Malay	69 (7.1)
	Indian	105 (10.8)
	Other	9 (0.9)
Family History	Diabetes	386 (39.7)
	Hypertension	267 (27.3)
	Ischaemic heart disease	113 (11.6)
	Stroke	105 (10.7)
Age at diagnosis in years	Mean	52.9
	Standard deviation	11.4
	Range	11 - 81
Duration since diagnosis (years)	Median	7.0
	Range	<1 - 40
History of hypertension	Present	448 (46.1)
	Diagnosed earlier than diabetes	188 (19.3)
	Diagnosed after diabetes	128 (13.2)
	Diagnosed same year as diabetes	98 (10.1)
	Year of diagnosis uncertain	34 (3.5)
Treatment	Dietary control	107 (11.0)
	Oral medications	817 (84.1)

the time of diagnosis were excluded from the study.

	Insulin	46 (4.7)
	Oral medications and insulin	8 (0.8)

Data collection included recording of information as documented in the patients' case records, such as the date at diagnosis, the history of hypertension, and the treatment given. Date of diagnosis of diabetes and hypertension were recorded to the nearest year. Family history of diabetes, hypertension and ischaemic heart disease in first degree relatives was obtained from patient interview.

Patients who had parents and/or siblings with known diabetes, hypertension or ischaemic heart disease were recorded as having a positive family history of these conditions. Five patients who did not know if their parents or siblings had such conditions, eg, orphans or those who were adopted and brought up by foster parents, were excluded from subsequent analysis.

Statistical analysis involved using Students t-tests and analysis of variance for comparing differences in mean ages of onset between patient subgroups, namely: those with and without family history of diabetes and history of hypertension; between males and females; and also among the three major ethnic groups. c2-tests were used for comparison of differences in proportions between the presence and absence of family history in different ethnic groups. Stratification by ethnic group was done for comparing the age at diagnosis between patients with and without family history of diabetes.

RESULTS

The descriptive profiles of the study subjects are shown in Table 1. The majority of the patients (81 per cent) belonged to the Chinese ethnic group. Male to female ratio was 1:1. Four out of 10 patients had a family history of diabetes, and three out of 10 patients had a positive family for hypertension. About half the study population had a history of hypertension. Mean age at diagnosis was 53 years (standard deviation: 11.4, range: 11-81 years). The patient who was diagnosed to have diabetes at age 11 years was treated with metformin for several years before secondary drug failure set in. He was then put on insulin.

Figure 1 displays graphically the frequency of patients with and without a family history of diabetes by age at diagnosis. It can be seen that more patients without a family history of diabetes were diagnosed later compared to patients with a positive family history.

In Table 2, the mean ages at diagnosis among patient subgroups were compared. There was no gender difference in the age of diagnosis. However, the mean age at diagnosis in patients with a positive family history was lower by seven years when compared to those without a family history. This difference was statistically significant. Among the different ethnic groups, the Malays and Indians had lower mean ages of onset when compared with the Chinese.

TABLE 2: MEAN AGE AT DIAGNOSIS BY PATIENT CHARACTERISTICS

Patient Characteristic		Age at Diagnosis		
		Mean	95% CI* of difference in means	p-value
Gender	Male	52.5		
	Female	53.1	-2.1 to 0.8	NS
Ethnic Group	Chinese	53.4		
	Malay	49.4		
	Indian	50.9	-	<0.01*
Family History of Diabetes	Present	48.6		
	Absent	55.7	5.7 to 8.5	<0.01
History of Hypertension	Present before diagnosis of diabetes	57.3		
	Absent	51.4	3.9 to 7.2	<0.01

* Significant difference between Malay and Chinese by post hoc tests
* Confidence interval

The diagnosis of hypertension preceding that of diabetes did not seem to lead to an earlier age of diagnosis of diabetes.

As a higher proportion of

Malays and Indians had family history of diabetes when compared to Chinese (Table 3), the relationship between family history and age at diagnosis was further examined by stratifying patients into three strata according to ethnic group. Among the Chinese, patients with a positive family history were diagnosed an average of seven years earlier compared to patients without a family history. The same was observed for Indian patients. These differences were statistically significant.

Among the Malays, although patients with a family history also had an earlier mean age at diagnosis compared to patients without a family history, the difference was smaller (four years), and this was not statistically significant. Malay patients without a family history of diabetes also had a lower mean age of onset when compared to Chinese (four years) and Indian patients (three years) without a family history.

TABLE 3: ASSOCIATION BETWEEN FAMILY HISTORY AND ETHNIC GROUP

Ethnic Group	Family History of Diabetes		95% CI * of difference in means	p-value
	Present	Absent		
Number (%) for each ethnic group				
Chinese	293 (37.1)	496 (62.9)		
Malay	35 (50.7)	34 (49.3)		0.03*
Indian	53 (50.5)	52 (49.5)		0.01*
Mean age at diagnosis				
Chinese	48.9	56.0	-8.7 to -5.6	<0.01
Malay	47.3	51.6	-9.7 to 1.1	0.12
Indian	46.9	55.0	-12.3 to -3.7	<0.01

* Significant difference in proportions when compared with Chinese
* Confidence interval

DISCUSSION

This study demonstrated that family history is an independent predictor of a lower age at diagnosis in patients with Type II diabetes. The association holds even within ethnic subgroups, though there were some ethnic differences with regard to the mean ages at diagnosis.

Statistical significance could not be established for the Malays because of the smaller difference in mean ages at onset, in addition to there being fewer Malay patients in the study population.

There were only 35 Malays with a positive family history and 34 without a family history. The power to detect a significant difference of 4.3 years in 69 subjects was only 0.5. The number of subjects required to increase the power to 0.8 would be 535. However, the authors are of the opinion that the difference of four years was of clinical significance.

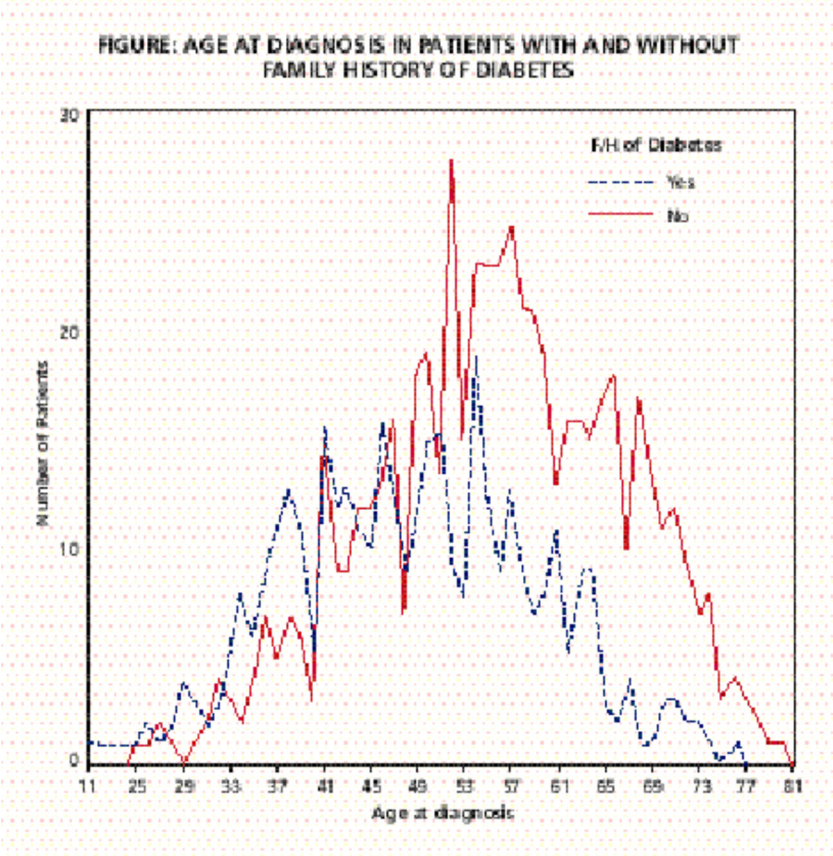
The absence of gender difference in age at diagnosis was also reported by Prishad, in his study of 2566 Iranian patients with non-insulin-dependent diabetes mellitus.[6]

There are several explanations for this observation of earlier diagnosis of diabetes in patients with a positive family history. Firstly, there could be a real difference in the ages of onset between these two groups of patients, resulting in an earlier age of diagnosis in patients with a positive family history. Mitchell et al[7] reported that, in Mexican-American families, family members of early-onset non-insulin-dependent diabetes patients had a five-fold higher risk of diabetes compared to those with later onset diabetes.

Secondly, subjects with family members who are diabetic could be more aware of the existence of the condition and more motivated towards screening for it, resulting in it being diagnosed earlier during the asymptomatic phase. Thirdly, they could be urged by their family members to go for earlier screening. In addition, physicians looking after diabetic patients could have encouraged the screening of family members for the presence of the disease.

Currently, in Singapore, screening for diabetes mellitus is targeted at individuals in the high risk groups.

In the recent report of the Expert Committee on the diagnosis and classification of diabetes mellitus,[8] screening for diabetes was recommended for all asymptomatic individuals aged 45 years and above, and at an earlier age for those with first degree relatives who have diabetes, among other risk factors.



Family physicians are well placed to play this role, in the earlier detection of diabetes in high risk individuals. In our study, patients with a positive family history were diagnosed about seven years earlier than those without a family history (48.6 v 55.7 years of age). Therefore, given the estimation that the onset of diabetes may precede its diagnosis by more than 10 years,[5] screening for family members of Type II diabetic patients should perhaps begin as early as when they are in their mid or late 30s.

As for the actual relationship between family history, age of onset and age of diagnosis, a prospective study could be carried out with yearly screening for diabetes in individuals with and without a family history of diabetes. This knowledge would contribute towards the understanding of the role of inheritance on the pathogenesis of Type II diabetes.

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