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ORIGINAL PAPER

Maternal Effect and Familial Aggregation in a Type 2 Diabetic Moroccan Population

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Abstract The aim of this study is to evaluate the degree of familial aggregation of type 2 diabetes mellitus in Morocco and to investigate transmission patterns of the disease and their relationships with patients' clinical profiles. Family history of diabetes and clinical data were collected from 232 unrelated type 2 diabetic Moroccan patients. Diabetes status was recorded for first degree (parents, siblings) and second degree relatives (aunts and uncles from both maternal and paternal sides). Among studied subjects, 50% reported at least one relative with diabetes and 24% had at least one parent with diabetes. Familial aggregation of type 2 diabetes was prominent and more important among first degree relatives than second degree relatives ($P < 0.01$). Moreover, diabetes was more frequent among mothers than fathers of probands ($P = 0.02$), but this maternal effect was not observed in second degree relatives. There are no significant differences in clinical and metabolic profiles between patients according to the transmission pattern of the disease. In conclusion, these results suggest familial aggregation and excess maternal transmission of type 2 diabetes in the Moroccan studied population.

Keywords Type 2 diabetes · Familial aggregation · Maternal transmission · Moroccans

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Introduction

Type 2 diabetes mellitus (T2DM) and associated complications pose a major health care burden worldwide and present a major challenge to patients, health care systems, and national economies. This disease is rapidly increasing with 366 million estimated affected persons worldwide in 2030 [1]. In Morocco, like in other developing countries, with the adoption of a new lifestyle of over-nutrition (mainly by saturated fat) and reduced physical activity, the prevalence of diabetes has increased dramatically, with an estimated 1.5 million affected persons in the range of 20–76 years old in 2030 [Diabetes Atlas] (http://www.diabetesatlas.org/map. Accessed in 25-5-2010).

T2DM is a multifactorial disease caused by a complex interplay of multiple genetic variants and environmental factors, leading to concomitant defects in both insulin secretion and insulin action [2]. T2DM belongs to the many complex diseases for which a genetic contribution is well accepted [3, 4]. The strong genetic component has been suggested by a high concordance rates of 60–90% in monozygotic twins [5] and by familial clustering studies [6, 7].

Several family studies reported that the risk of diagnosed T2DM increases when one or both parents are affected [8, 9], and some studies suggest that persons

whose mothers had diabetes are more likely to develop diabetes themselves, compared with persons whose fathers had diabetes [10, 11].

Studying the family clustering of T2DM in our population can give insight to understand mechanisms underlying parental influences. To our knowledge, in North Africa just one study on familial aggregation of T2DM and transmission patterns have been reported [12], but none in Morocco. The objective of this study was to assess the degree of familial aggregation of T2DM in the Moroccan population and to investigate transmission patterns of this disorder and their relationships with patients' clinical characteristics.

Materials and Methods

Subjects

Subjects with type 2 diabetes were recruited randomly at the department of metabolic diseases in the UHC Ibn Rochd, Casablanca, Morocco. The subjects were briefed on the study procedures, and written consent was obtained before study participation. This study was approved by the institutional ethical committee.

A sample of 232 (Sex ratio: 78 Man/154 Woman) unrelated Moroccan patients with T2DM was enrolled; all patients were from various geographic regions of the country: North, South, East, West, and Middle, and the ethnic background of subjects included Arab, Berber, and Sahraoui. T2DM was diagnosed according to World Health Organization (WHO) criteria. Clinical and biochemical parameters were determined (Age at diabetes diagnosis, body mass index (BMI), blood pressure, cholesterol, triglyceride, and glucose levels). Patients were interviewed about their family history of diabetes. All participants responded to an interview following a detailed questionnaire regarding the diabetes status of their parents, siblings, uncles and aunts from both maternal and paternal sides. Diabetic relatives were classified into two groups: first degree for parents and siblings and second degree for uncles and aunts.

Statistical Analysis

The maternal effect was first tested among parents (mother vs. father) and then among aunts and uncles (maternal vs. paternal side). Comparison of proportions was performed by χ^2 test (Mc Nemar). To assess differences in the metabolic parameters between patients according to their parents' diabetes status, Student t test was used for comparison of two means with a value of $P < 0.05$ considered as statistically significant.

Results

Frequency of Diabetes Among Patient's Relatives

All cases with at least one uncertain or unknown relative diabetes status were excluded. From a total of 300 patients with T2DM, 232 completed the questionnaire and complete data sets on family history of diabetes (mothers, fathers, sisters, brothers, aunts and uncles from both maternal and paternal sides) were obtained. Details for patients of this study are given in Table 1.

Diabetic relatives were classified into two groups: first degree for parents and siblings and second degree for uncles and aunts.

From our cohort of 232 patients, 116 (50%) had at least one affected relative and 57 (25%) had at least two diabetic family members. When classifying these relatives according to first and second degree, 105 (45%) reported at least one diabetic parent or sibling, 32 (14%) had at least one affected uncle or aunt from either maternal or paternal side and 21 (9%) had both first and second degree relatives with

Table 1 Clinical and laboratory characteristics of the all patients of this study and the patients with diabetes in the mother or the father

Variable[a]	All diabetes (*N* 232)	Parental diabetes (−)	
		Maternal (*N* 33)	Paternal (*N* 16)
Age at diagnosis (year)	57.6(11.12)	54.4(11)	54.5(11.2)
Age beginning diabetes (year)	50.78(12)	50.6(11.59)	50.7(12)
BMI (kg/m^2)	28(5)	28(5)	27.94(4.9)
Fasting plasma glucose (g/l)	1.8(0.78)	1.99(0.79)	1.99(0.79)
Triglycerides (g/l)	1.4(0.7)	1.34(0.72)	1.34(0.73)
Total cholesterol (g/l)	2(0.45)	1.96(0.45)	1.95(0.46)

BMI body mass index

[a] Values of all parameters are given as mean (SD)

(−) There is no significant difference in clinical and biochemical characteristics between patients with paternal or maternal history of diabetes

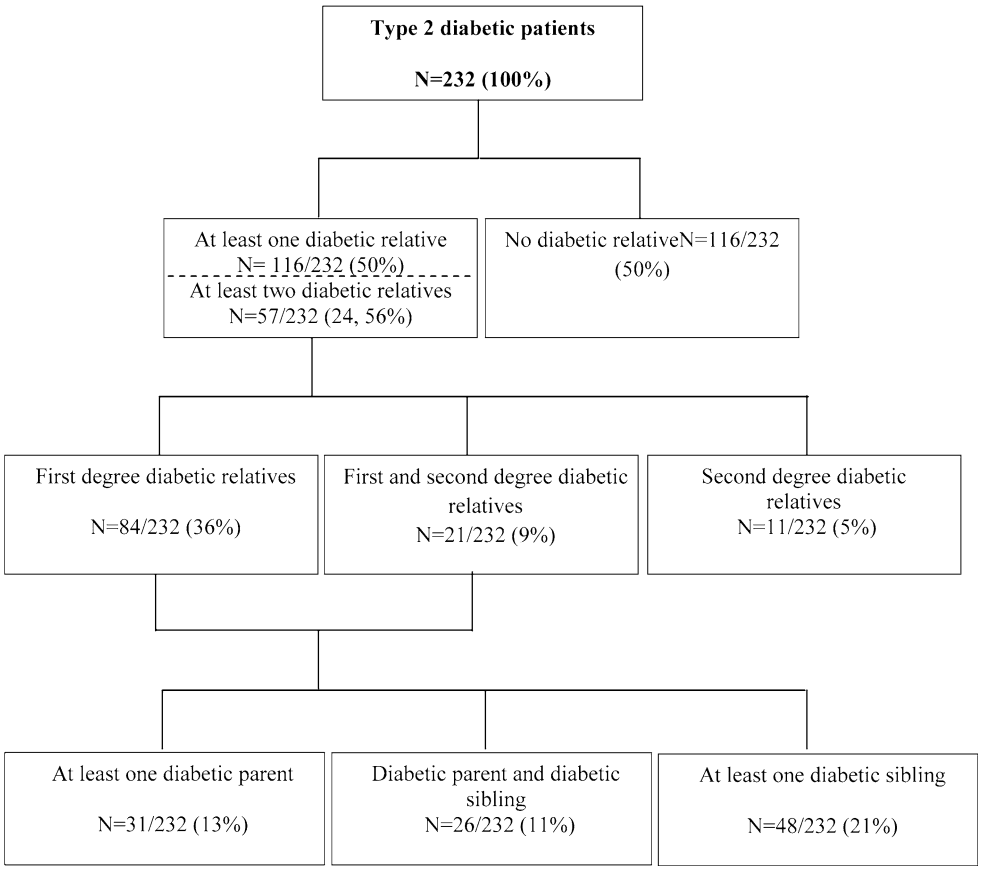

Fig. 1 Family history of diabetes. Flow chart showing the frequency of diabetes in relatives. Data are number (percentage in parentheses) of index patients having at least one first or second degree relative with diabetes

diabetes. Overall patients with positive history of diabetes in first degree relatives, 57 (25%) had at least one diabetic parent, 74 (32%) had at least one diabetic sister or brother and 26 (11%) had at least one diabetic parent and sibling. We found that 36% of first degree relatives are affected compared to 5% of second degree relatives ($P = <0.01$), suggesting a prominent familial aggregation of T2DM. The frequencies of diabetic relatives are given in Fig. 1.

Maternal Effect

Patients were divided according to their parent's and uncles/aunt's status respectively in order to estimate the parental transmission of T2D. Results showed that among the 232 diabetic subjects, 57 (25%) had at least one parent with diabetes, 33 (14%) had only an affected mother (maternal), 16 (7%) had only a diabetic father (paternal) and 8 (4%) had both parents affected (bilineal; Fig. 2a). In the another hand, 32 (14%) had at least one diabetic second degree relative with diabetes, 18(8%) from them had only diabetic maternal aunts or uncles and 13(5.6%) had only diabetic paternal aunts or uncles (Fig. 2b). In conclusion, patients were more likely to have a mother with diabetes than a father with diabetes (14% vs. 7%, respectively $P = 0.02$), but we did not find a difference in second degree relatives (8% vs. 5.6%, respectively, $P =$ NS). These results suggest an excess of maternal transmission of T2DM that don't extend to the second degree relatives.

Influence of the Parental Transmission of T2DM on the Clinical and Metabolic Parameters

We examined the influence of various transmission patterns of T2DM on clinical and metabolic parameters (age at diagnosis, BMI, fasting plasma glucose, triglycerides, total cholesterol). The probands were classified in two groups: maternal (if only the mother had diabetes) or paternal (if only the father had diabetes). Results showed no significant differences in clinical parameters between patients with paternal or maternal history of diabetes in the studied sample (Table 1).

Discussion

Changing lifestyle and increasing urbanisation increased the number of Moroccan with diabetes mellitus as for many other Arab countries [13]. In Morocco the prevalence of type 2 diabetes is not known with exactitude, but many studies in different regions of the country gave an estimation of 2.26%

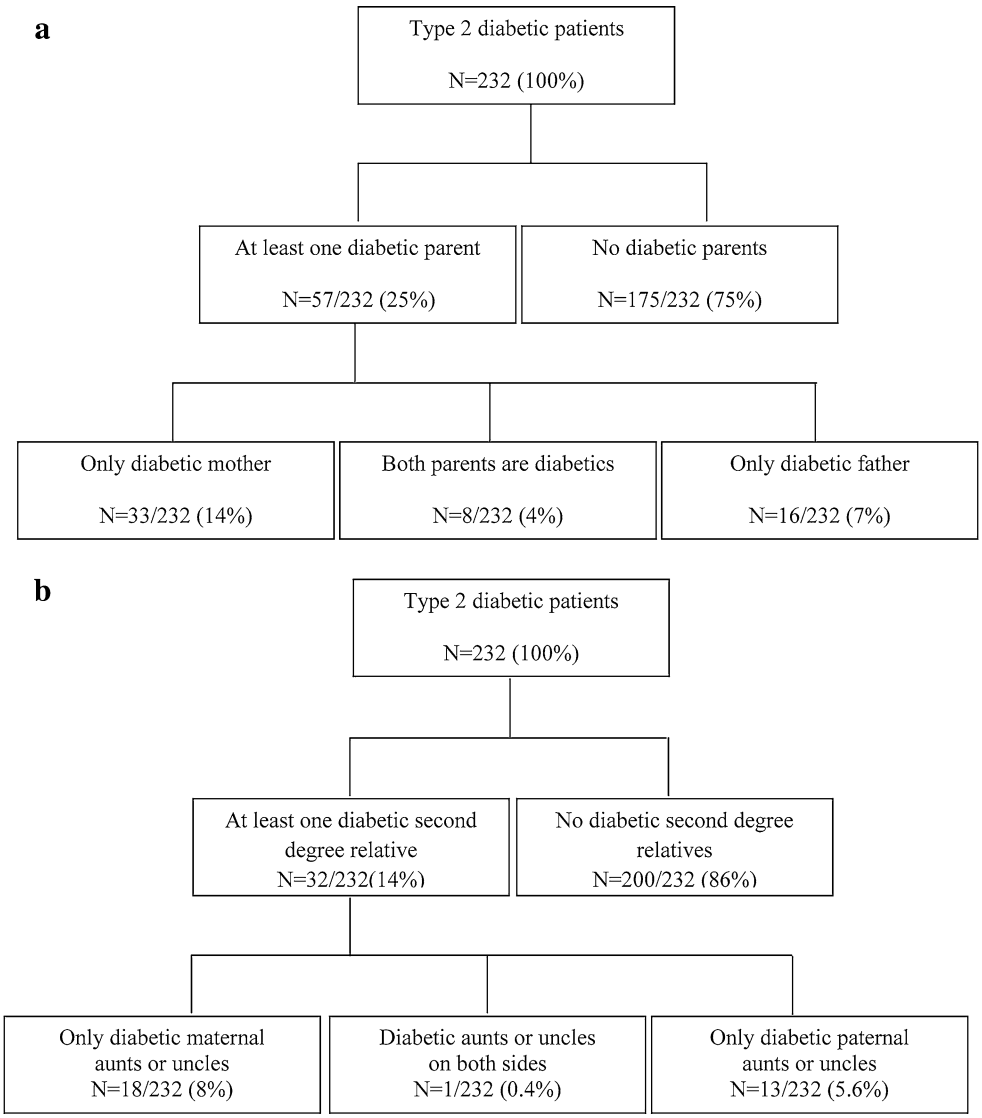

Fig. 2 Assessment of the maternal effect. Flow chart showing the frequency of diabetes in relatives on maternal and paternal sides. Data are number (percentage in parentheses) of probands having **a** parents with diabetes and **b** second degree relatives with diabetes; $P = 0.02$ for mother vs. father, $P =$ NS for maternal aunt/uncle vs. paternal aunts/uncles

[14, 15]. The complications resulting from this disease are associated with the damage or failure of large and small blood vessels and are a significant cause of morbidity and mortality [16, 17]. Therefore, the early diagnosis of type 2 diabetes has a major importance as the normalisation of glycaemia may reduce the risk of complications [18]. For these reasons, we studied the degree of familial aggregation and parental transmission in Moroccan population. To our knowledge, this is the first study investigating the familial aggregation and transmission patterns of T2DM in Morocco and the second in North Africans, the first one concerned the Tunisian population [12].

In this study, we observed that 50% of the subjects with diabetes had a positive family history of diabetes among at least one of their parents, siblings, uncles and aunts from both sides. This result supports familial aggregation of diabetes, as reported in several populations with varying frequencies. In Greek population 53.6% reported a family history of type 2 diabetes [19], In the French CODIAB study, 66% had at least one diabetic relative [20], 33% of diabetics in the Whitelhall study had a diabetic family member, and among 300 T2DM patients from Cheta, 33% had a diabetic relative [21, 22].

In Africa, Mengesha and Abdulkadir reported a significant positive history in first, second, and third degree relatives of Ethiopian diabetics [23]. In South Africa, Erasmus et al. reported that 27.3% of the diabetic subjects reported at least one diabetic family member [24]. In Tunisia, 70% of the subjects with diabetes had a positive family history of diabetes [18]. In our study, we found that 36% of the first degree relatives are affected compared to 5% of the second degree relatives ($P = 0.0001 < 0.01$). The result found in our study confirms the high heritability of T2DM diabetes in our population.

In this study, we also investigated the parental transmission of T2DM, we found an excess of maternal transmission of type 2 diabetes as mothers were implicated two times more frequently than fathers, but this result is not observed in second degree relatives.

The excess maternal transmission of T2D reported in the present study is in line with studies from different populations (Greek, Tunisian, English, French, black South African, Chinese, North American, Italian and Brazilian) [7, 9, 12, 19, 20, 24–27], although other studies reported no difference in parental transmission of T2DM [6, 28, 29].

To explain the excess maternal transmission of T2D several potential genetic and environmental factors have been proposed. Studies reported that the intrauterine environment may contribute to the maternal influence [30, 31]. Offsprings of Pima Indian women are more likely to develop diabetes if their mothers were diabetic during the pregnancy, than if the mothers develop diabetes later in life [32]. Also genetic defects such as mutations in mitochondrial genome [33] and other genetic factors allowing low birth weight babies to survive may also be implicated [34]. All these factors may contribute to increase susceptibility to diabetes, especially in the presence of a sedentary and high-fat food abundant lifestyle. Potential reported biases can also explain the excess maternal transmission of T2DM such as the fact that fathers of diabetic subjects may be more likely to die of insulin resistance associated with cardiovascular disease before onset of T2DM than mothers [35]. The hypothesis that individuals may have more knowledge about their mothers' health status than they do about their fathers' could further contribute to this disequilibrium. But this should not be the case in our study because of cultural background and because all cases with missing or being uncertain about their parents status were excluded.

The influence of the various transmission patterns of T2DM on clinical and metabolic factors showed no significant difference between the patients with paternal or maternal history of diabetes. This result was found in many different studies [12, 25], but others showed a positive association between maternal history of diabetes and lipid profiles [36, 37].

Conclusion

The data for our study were collected in the Ibn Rochd health centre of Casablanca, which is a referral health centre in Morocco for T2DM. All the patients included in this study were from different ethnic groups (Arab, Berber and Sahraoui); consequently, we think that we can extrapolate our results to the total Moroccan population and that they can form a platform for prospective genetic studies in Morocco. Further molecular investigations of candidate genes will help to better evaluate the aetiology of the maternal effect of type 2 diabetes.

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Conflict of interest The authors declare that they have no conflict of interest.

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