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Research Article

To study the pattern of inheritance and its association with micro and macrovascular complications in patients of Type 2 DM from central India

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Abstract
Background: *Diabetes mellitus (DM) is multi-factorial polygenic disease resulting from interaction of both genetic and environment factors. Diabetes mellitus is known to have strong genetic inheritance and familial influence. Maternal and paternal diabetes conferred equivalent risk for occurrence of type 2 diabetes mellitus in offspring.*
Methods: *The total of 100 patients of type 2 DM attending outdoor and indoor patient department, were enrolled in this study.*
Results: *Mean age was 57 year, 55% cases were female out of which 61% were having positive family history of DM. 45% cases were male out of which 39% were having positive family history of DM. Comorbid hypertension (HTN) was present in 72%, out of which 62% patients were showing positive family history of HTN and it was statistically significant(p value= 0.01) high as compare to patients who had no family history of HTN. A total 28% patients had comorbid CAD, out of which 75% had positive family history of CAD and it was statistically significant(p value=0.01). Microvascular complications like nephropathy, neuropathy and retinopathy were present in 13%, 14% and 24% respectively. The family history of microvascular complications like nephropathy, neuropathy and retinopathy were present in 84%, 85% and 75% respectively and all were statistically significant(p value<0.05).*
Conclusions: *Using family history and pedigree charting as a screening tool is appealing for early diagnosis of DM and its specific micro and macrovascular complications. Prevention of DM and its complications can be targeted to the individual by dietary advice, weight reduction, physical exercise healthy habits, and lifestyle modification.*
Keywords: *Diabetes mellitus, Macrovascular complications, Microvascular complications.*

Introduction

Diabetes mellitus is multi-factorial polygenic disease resulting from interaction of both genetic and environment factors[1]. It is important to analysis the epidemiology of the disease. Diabetes is known to have strong genetic inheritance and familial influence. There is an increase in the percentage of population being exposed to diabetes in addition to the decrease in age of onset[2]. It is therefore becomes important to analyse the epidemiology of the disease. In framingham population study maternal and paternal diabetes conferred equivalent risk for occurrence of Type 2 diabetes mellitus in offspring. While existence of excess of maternal transmission of Type 2 diabetes mellitus was observed in the analysis carried out in Northern California[3]. In this study we have examined consecutive Type 2 diabetic patients from a tertiary level Govt. Medical College hospital, situated in central part of India from the point of view of familial paternal transmission, age of onset, as well as pattern of inheritance of diabetes with respect to maternal or paternal transmission etc.

Methods

A cross section observational study was carried in the Department of Medicine, M.G.M. Medical College, Indore, Madhyapradesh, India, during period of March 2017 to February 2018. The study was approved by Ethical Committee of M.G.M. Medical College, Indore, Madhyapradesh, India. The total of 100 patients of Type 2 DM attending OPD and IPD, M.Y. Hospital, Indore were enrolled in this study. A detailed history was elicited from all patients with emphasis on duration of diabetes mellitus, age of onset, symptomatology of diabetes mellitus and its various micro-angiopathic complications, interviewed for family history in addition to the study of medical records of the patients. Analysis of the pedigree data was carried out with help of family history. Statistical analysis of the data was carried out using Chi-square test.

Eligibility criteria

All consecutive patients having history of type 2 diabetes mellitus, who provided informed valid written consent for participation.

Exclusion criteria

Patients not given consent, below 18 years of age, patients having history of type 1 DM patients having history of gestational DM and secondary DM were excluded from this study.

Criteria for diagnosis of DM

- Diabetes Mellitus was defined on the basis of serum fasting glucose levels 126 mg/dl and/or serum post prandial 2 hour glucose level 200 mg/dl or HBA1c ≥6.5% or insulin or oral anti-diabetic drugs treatments.

Criteria for diagnosis of HTN

- Systolic BP ≥130mm of Hg and/or Diastolic BP ≥80mm of Hg or on antihypertensive drugs.

Diagnosis of coronary artery disease

- Angiographically proven CAD and/or
- Cardiac enzyme elevation was considered as positive marker for myocardial infarction if value was raised above 99th percentile and/or
- On ECG, new ST elevation at the J point in two contiguous leads with the cut point: ≥1mm in all leads other than leads V2-V3 where the following cut points apply: ≥2mm in men ≥40years; ≥2.5mm in men<40years, or ≥1.5mm in women regardless of age. ST segment depression and T wave changes were defined as new horizontal or down sloping ST– depression ≥0.5mm in two contiguous leads and/or T inversion >1mm in two contiguous leads with prominent R wave.

Results

In this study, as shown in table 1, out of total 100 Type 2 DM patients, 45(45%) were males and 55(55%) were females with mean age of 57 years.

8(8%) patients in the study were in the age group of 30-40 years, in which 3 were males and 5 were females. 21(21%) patients were in the age group of 41-50 years, in which 9 were males and 12 were females. 39(39%) patients in the study were in the 51-60 age group, in which 19 were males and 20 were females. 22 patients (22%) were in the age group of 61-70 years, in which 10 were males and 12 was female. 4 patients (4%) in the study were in the age group of 71-80 years. Of these 4 were males and 6 were female. Most patients were between the age group 51-60 years (39%). Mean ages were 57 years; Median ages were 56 years and range 35 to 80 years.

Table 1: Age and gender wise distribution of patients

Age Groups in Years	Gender		Total	Percentage
	Male	Female		
30-40	3	5	8	8%
41-50	9	12	21	20%
51-60	19	20	39	39%
61-70	10	12	22	22%
71-80%	4	6	10	10%
Total	45	55	100	100%

As shown in the table 2, total 55(55%) cases were female and out of those 33(61%) were having positive family history and, 45(45%) cases were male and out of those 21(39%) were having positive family history.

Table 2: Prevalence of family history in both male and female

Sex	Total no. of cases	Positive family history	Percentage of positive family history
Male	45	21	39%
Female	55	33	61%
Total	100	54	100%

As shown in the table 3, the most common associated disease with Type 2 DM was hypertension, which was present in 72(72%), in which 45(62%) patients were showing positive family history and it was significantly (p value=0.01, chi square value 6.3) high as compare to patients of DM who had no family history of DM. A total 28(28%) patients had CAD, in which 21(75%) had positive family history of DM and it was statistically significant (p value=0.01, chi square value 5.78) as compare to patients without family history of DM. Microvascular complications like nephropathy, neuropathy and retinopathy were present in 13(13%), 14(14%) and 24(24%) respectively. The family history of microvascular complications like nephropathy, neuropathy and retinopathy were present in 11(84%) (p value=0.03, chi square value 4.3), 12(85%)(p value=0.02, chi square vale 5.19) and 18(75%)(p value=0.03, chi square value 4.54) respectively and all were statistically significant (p value<0.05). Thyroid disease was present in 5(5%) patients, out of which 4(80%) patients had family history and it was statistically non significant (p value=0.46, chi square value 0.54). A total 10(10%) patients had history of CVA, in which 7(70%) patients had positive family history and it was non statistically significant (p value=0.46, chi square value 0.54).

Table 3: Association between complications of DM and family history

Associated disease/ complications	Total Number	Positive Family history	% of Positive family history	p value
Hypertension	72	45	62%	0.01
CAD	28	21	75%	0.01
CVA	10	7	70%	0.46
Nephropathy	13	11	84%	0.03
Neuropathy	14	12	85%	0.02
Retinopathy	24	18	75%	0.03
Thyroid Disease	5	4	80%	0.46

Inheritance of type 2 DM in family members i.e. father, mother and both parents, the prevalence was 16.7%, 14.8% and 11.11% respectively. In offspring's i.e. son, daughter and both, the prevalence of Type 2 DM was 9.3%, 5.5% and 0% respectively and the prevalence of Type 2 DM in grandparent was 5.5% as shown in table number 4.

Table 4: Inheritance of DM in family members

Positive family history	Father	Mother	Both parents	Grand parents	Brother	Sister	Broth-er & Sister	Son	Daughter	Both Son & Daughter
54	9	8	6	3	16	16	8	5	3	0
%	16.7%	14.8%	11.11%	5.5%	29.6%	29.6%	14.11%	9.3 %	5.5%	0%

Discussion

Type 2 DM has a strong genetic component. The concordance of Type 2 DM in identical twins is between 70 and 90%. Individuals with a parent with Type 2 DM have an increased risk of diabetes.

In the present study out of 100 patients, 45(45%) were males and 55(55%) were females with mean age of 57 years. Most patients were between the age group 51-60 years (39%). Mean ages were 57 years; Median ages were 56 years and range 35 to 80 years. Positive family history was present in 33(61%) out of 55 female diabetic patients and 21(39%) out of 45 male diabetics. These findings suggest that inheritance of Type 2 DM is more common with female sex as compare to male sex. A study done by Andrew J. Kartar et al[3], also found that inheritance of Type 2 DM was more common from mother to their offspring (20%) as compare to father (17%). As compare to this study, our study showed inheritance of Type 2 DM in female and male was 61% and 39% respectively. A study done by Meigs JB et al[4], found that maternal Type 2 DM were slightly more likely to have diabetes as compared with those with paternal diabetes.

The most common associated disease with Type 2 DM was hypertension, which was present in 72(72%), in which 45(62%) patients were showing positive family history of DM. A total 28(28%) patients had CAD, in which 21(75%) had positive family history and it was significantly high (p value= 0.01) in patients with positive family history. A total 10(10%) patients had history of CVA, in which 7(70%) patients had positive family history and it was non significantly (p value=0.46) correlated with positive family history. Microvascular complications like nephropathy, neuropathy and retinopathy were present in 13(13%), 14(14%) and 24(24%) respectively. The family history of microvascular complications like nephropathy, neuropathy and retinopathy were present in 11(84%) (p value=0.03), 12(85%)(p value=0.02) and 18(75%) (p value=0.03) respectively and all are statistically significantly(p value<0.05) high in patients with family history. Thyroid disease was present in 5(5%) patients, out of which 4(80%)

patients had family history and it was statistically non significant (p value=0.46). Both the macrovascular and microvascular complications were high in patients who had positive family history. This could be due to early onset development of Type 2 DM in patients who had positive family history. Patients with positive family history of Type 2 DM, leads to early development of diabetes in offspring lead to more macrovascular and microvascular complications and with greater extent. Thus by early diagnosis of diabetes and its complications by tracing inheritance pattern in other family members we control disease severity and irreversible complications.

Conclusion

This study reflexed a strong genetic association of Type 2 DM and its specific microvascular and macrovascular complications. Specific microvascular complication like retinopathy, nephropathy and neuropathy had strong genetic association with positive family history of Type 2 DM with respective complications. Non specific macrovascular complications like CAD had strong genetic association with positive family history of Type 2 DM with CAD. Comorbid condition like HTN also had strong genetic predilection with positive family history of Type 2 DM with HTN in the family member. Thus our study revealed that not only the DM but its specific complications like retinopathy, nephropathy and neuropathy as well as non specific complication like CAD had statistically significant familial clustering due to genetic association.

Using family history and pedigree charting as a screening tool is appealing for early diagnosis of DM and its specific microvascular and macrovascular complications. Prevention of DM and its complications can be targeted to the individual by dietary advice, weight reduction, physical exercise healthy habits, and lifestyle modification.

Declarations

Funding: No funding sources

Conflict of interest: Not declared

Ethical approval: The study was approved by the institutional ethics committee

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