Study of Inheritance of Diabetes Mellitus in Western Indian Population by Pedigree Analysis

Sonali S Deo*, SD Gore**, DN Deobagkar*,***, Deepti D Deobagkar*,***

Abstract

Objectives: To study the inheritance pattern of diabetes mellitus in Western Indian population by analysing the pedigree of diabetes patients.

Methods: 3,921 individuals from 300 families were interviewed for family history in this study, out of which 770 were diabetic individuals. Statistical analysis of the data was carried out using T-test and Chi-square test.

Results: 37% cases of Type 1 DM and 58% cases of Type 2 DM showed family history of the disease. Of the cases showing family history for diabetes, 92% in case of Type 1 DM and 59% in case of Type 2 DM showed family history of Type 2 DM with a decrease in age of onset in the successive generations. Both the parents, when diabetic conferred equal risk of inheriting diabetes in offspring. The sex ratio of offspring suffering from diabetes was not influenced when only one of the parents was diabetic. However, it was observed that the male offspring were highly susceptible when both parents were diabetic (Chi-square value = 4.55 with 1 d.f.). The age of onset of diabetes did not show significant correlation with whether one or both the parents were diabetic. However, it was noteworthy that in case of familial history of diabetes there was a decrease in the age of onset in successive generations.

Conclusion: This study suggests that family history of diabetes results in predisposition to early onset of the disease in successive generations and a cluster of genes involved in Type 2 DM may show a parental effect for predisposition to Type 1 DM in the offspring in this set of Indian population.

INTRODUCTION

Diabetes mellitus is a multifactorial disease resulting from interaction of both genetic and environmental factors.1,2 Type 2 DM is the commonest form of diabetes (90-95% of the diabetes population) resulting from insulin resistance combined with relative insulin deficiency. Type 1 DM is an autoimmune disease, which accounts for 5-10% of diabetic cases.

In the year 2000, ~171 million people were estimated to be diabetic worldwide, which is projected to rise to 366 million in 2030 3. India was estimated to have the highest number of diabetes cases in 2000 – 31.7 million and by 2030 it is estimated to rise to 79.4 million.7 There is an increase in the percentage of population being exposed to diabetes in addition to the decrease in age of onset. It therefore becomes important to analyse the epidemiology of the disease.

Diabetes is known to have a strong genetic component. There is a familial influence on the frequency of diabetes.4

In Framingham population study maternal and paternal diabetes conferred equivalent risk for occurrence of Type 2 DM in offspring 5 while existence of excess of maternal transmission of Type 2 DM was observed in the analysis carried out in Northern California.6 Familial clustering of diabetes and a significant maternal influence as well as a male sex-specific paternal effect was reported in a Chinese population study.7

In this study we have examined a population in Maharashtra, India from the point of view of familial background and disease occurrence as well as pattern of inheritance of diabetes with respect to maternal or paternal transmission, age of onset etc.

MATERIALS AND METHODS

This study was carried out with the help of Diabetic Association of India, Pune branch. Diabetic patients diagnosed according to the WHO criteria8 were interviewed for family history and age of onset of the disease, in addition to the study of medical records of the patients. Written consent was obtained from all the patients participating in the study. 3,921 individuals from 300 families were considered for this study, out of which 770 were diabetic individuals. Analysis of the pedigree data was carried out with help of previously
developed database for diabetes patient data and statistical methods using T-test and the Chi-square test.

RESULTS

In the population being analysed, there were 5% Type 1 DM patients (Table 1) while 95% were Type 2 DM patients. In case of Type 1 DM 38% patients were males and 62% were females, while 53% Type 2 DM cases were males and 47% were females.

Table 1: Incidence of diabetes mellitus

<table>
<thead>
<tr>
<th>Total Type 1 DM</th>
<th>Total Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>733</td>
</tr>
<tr>
<td>Type 1 DM males</td>
<td>14</td>
</tr>
<tr>
<td>Type 1 DM females</td>
<td>23</td>
</tr>
<tr>
<td>Type 2 DM males</td>
<td>391</td>
</tr>
<tr>
<td>Type 2 DM females</td>
<td>342</td>
</tr>
</tbody>
</table>

In case of Type 1 DM highest number of patients (62%) had age of onset between 11 to 20 years (Table 2, Fig. 1). Highest number of Type 2 DM patients (66%) had age of onset between 41 to 60 years (Table 3, Fig. 2).

Table 2: Age of onset of Type 1 DM

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of Males</th>
<th>Percentage</th>
<th>No. of Females</th>
<th>Percentage</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 10</td>
<td>5</td>
<td>36</td>
<td>4</td>
<td>17</td>
<td>24</td>
</tr>
<tr>
<td>11 to 20</td>
<td>7</td>
<td>50</td>
<td>16</td>
<td>70</td>
<td>62</td>
</tr>
<tr>
<td>21 to 30</td>
<td>2</td>
<td>14</td>
<td>3</td>
<td>13</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 3: Age of onset of Type 2 DM

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of Males</th>
<th>Percentage</th>
<th>No. of Females</th>
<th>Percentage</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 to 30</td>
<td>10</td>
<td>3</td>
<td>11</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>31 to 40</td>
<td>81</td>
<td>21</td>
<td>69</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>41 to 50</td>
<td>143</td>
<td>37</td>
<td>116</td>
<td>34</td>
<td>35</td>
</tr>
<tr>
<td>51 to 60</td>
<td>118</td>
<td>30</td>
<td>107</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>61 to 70</td>
<td>36</td>
<td>9</td>
<td>30</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>3</td>
<td>1</td>
<td>9</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

When the data was analysed for pattern of inheritance, it showed that both the parents conferred equal risk of inheriting diabetes in offspring (Chi-square value = 1.11 with 1 d.f.). There was not a significant difference between the age of onset of diabetes depending on whether only father was diabetic (P-value = 0.354), only mother was diabetic (P-value = 0.378) or both the parents (P-value = 0.437) were diabetic. Also both sons and daughters were equally affected when only the mother was diabetic (Chi-square value = 1.76 with 1 d.f.) or the father was diabetic (Chi-square value = 0.009 with 1 d.f.). However when both the parents were diabetic, male offspring were more susceptible to diabetes (Chi-square value = 4.55 with 1 d.f.).

37% of Type 1 DM cases showed a family history of Type 2 DM while remaining 63% had no record of diabetes history in the family (Table 4). In case of Type 2 DM 58% of the cases showed diabetes family history, 28% cases had no family history of diabetes and in case of 14% cases, family history was not known.

Table 4: Family history of diabetes

<table>
<thead>
<tr>
<th>Type 1 DM</th>
<th>Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of families</td>
<td>Percentage</td>
</tr>
<tr>
<td>Diabetes family history</td>
<td>13</td>
</tr>
<tr>
<td>No family history</td>
<td>22</td>
</tr>
<tr>
<td>Not known</td>
<td>0</td>
</tr>
</tbody>
</table>

Age of onset – Patterns

We categorised age of onset patterns into five different categories (Table 5).

- Increased – Age of onset of diabetes increased in the successive generations. (Fig. 3a)
- Decreased – Age of onset of diabetes decreased in the successive generations. (Fig. 3b)
- Same – Age of onset of diabetes remained almost same in all generations. (Fig. 3c)
- No pattern – No definite pattern observed in the generations. (Fig. 3d)
- Only one generation affected. (Fig. 3e)

Of the cases showing family history for diabetes, 92% in case of Type 1 DM and 59% in case of Type 2 DM
Fig 3: The probands are indicated with an arrow. Arabic numbers below the symbol indicate the age of onset of diabetes mellitus. Not affected; Diabetes mellitus.

(a) Increased age of onset in successive generations; (b) Decreased age of onset in successive generations; (c) Same age of onset in successive generations; (d) No pattern of onset in successive generations; (e) Only one generation affected.

showed family history of Type 2 DM with a decrease in age of onset in the successive generations (Table 5).

### Table 5: Age of onset pattern

<table>
<thead>
<tr>
<th></th>
<th>Type 1 DM</th>
<th></th>
<th>Type 2 DM</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of</td>
<td>Percentage</td>
<td>No. of</td>
<td>Percentage</td>
</tr>
<tr>
<td>1- Increased</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>2- Decreased</td>
<td>12</td>
<td>92</td>
<td>92</td>
<td>59</td>
</tr>
<tr>
<td>3- Same</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>4- No pattern</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>5- No pattern</td>
<td>1</td>
<td>8</td>
<td>30</td>
<td>19</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Diabetes is a disease that has a strong clustering in families and has a genetic component. However, environmental factors such as diet and oxidative stress equally contribute to the disease occurrence. When the patterns of inheritance of diabetes were analysed in different populations, specific trends were observed in these sets of population with respect to different parameters e.g., excess of maternal transmission, lack of excess of paternal transmission, male sex specific paternal effect, maternal and paternal diabetes conferring equivalent risk, and so on. Thus there is a familial influence on the transmission of diabetes and different genetic and environmental factors contribute to the transmission of disease in different populations and influence penetrance, variability and epidemiology.

In the present analysis related to patterns of transmission in western Indian population the following salient features were observed. Age of onset of Type 1 DM in 62% patients was between 11 to 20 years; where females were more affected (70%) than the males (50%). In case of Type 2 DM 35% of the patients were reported to have an age of onset between 41 to 50 years. Here the percentage of males (37%) and females (34%) did not show a significant difference in this age group. This suggests that incidence of Type 1 DM was more in females than males but in case of Type 2 DM, both the sexes were equally affected in this set of population.

37% of Type 1 DM cases showed a family history of Type 2 DM. While remaining 63% had no known diabetes history in the family. On the contrary, in the case of Type 2 DM, larger number of patients had a diabetes family history (58%). The onset of Type 1 DM in majority of the cases, thus could be due to spontaneous mutations or due to environmental effects in this set of population. A certain percentage of Type 1 DM cases showed previous history of Type 2 DM in the family. This study thus suggests a cluster of genes involved in Type 2 DM may show a parental effect for predisposition to Type 1 DM in the offspring.

Both in case of Type 1 DM and Type 2 DM there was a decrease in age of onset when there was a previous history of diabetes in the family. This suggests that the presence of diabetes in the family results in predisposition to diabetes in subsequent generations. Predisposition for the early age of onset observed in this analysis in cases where there was a family history of diabetes, suggests clustering of different sets of mutations which could be responsible for Type 2 DM in different families.

Thus this set of population in western India showed the following features. Age of onset of diabetes decreased with generations in families with history of diabetes, both the parents conferred equal risk in transmission of diabetes as previously reported in Framingham offspring study; and sons were more susceptible to the disease when both parents were diabetic. In this study we also observed absence of excess of maternal transmission as previously reported in the Korean population and the south Indian population. The pedigree analysis of genetic transmission thus gives valuable insight into genetic epidemiology and leads to better understanding of the pattern of occurrence of diabetes. The involvement of multiple genes and mutations in occurrence of diabetes reported earlier could influence the inheritance patterns observed. These variations in the transmission pattern could be related to the clustering of different mutations in the gene pool.

**Acknowledgements**

We acknowledge the financial support from University Grants Commission and Department of Science and Technology FIST Grant from Government of India, New Delhi. The generous help and support from Dr. Ramesh Godbole and Diabetic Association of India, Pune branch is gratefully acknowledged.
REFERENCES


---

**Announcement**

**IMSACON 2006**

Annual Conference of International Medical Sciences Academy **IMSACON 2006** will be held on 3, 4, 5th November, 2006 at Lahore (Pakistan).

**Theme:** “Update in Medical and Dental sciences”

**Venue:** Lahore Hospital and Dental Medical College, Canal Bank North, Tuls pura, Lahore, 53400, Pakistan.

For further details contact:

IMSA CON 2006

**Conference Secretariat**

Prof. Shaheena Asif

Organizing Secretary IMSACON 2006

Surgimed Hospital

1-Zafar Ali Road, Lahore Pakistan

Phone : (92-42) 5714411-8,

Mobile : (92-300) 848 6336

E-mail : shaheena@nexlinx.net.pk

International Medical Sciences Academy

**World Headquarter (MSA)**

Dr. H.K. Chopra

Secretary General

International Medical Sciences Academy

2nd Floor, National Medical Library Building,

Ring Road, Ansari Nagar, New Delhi - 110029

Ph : 26589660, 26588226, Mobile : 9811090204

E-mail : imsahq@ndf.vsnl.net.in

---

**Announcement**

**Indian Society of Electrocardiology**

**Aligarh Arrhythmia Course - 2006 (AAC-2006)**


For further details, contact : Dr. KK Varshney, Organizing Secretary, AAC 2006, KK Hospital and Heart Centre, Ramghat Road, Aligarh (UP) 20200.

Ph : 0571-2741062, 3090757 Telefax : 0571-2741061

Mobile : 09358258116 E-mail : varshneykk5@yahoo.com

Dr. SB Gupta, Hon. Secretary, Indian Society of Electrocardiology, Head Department of Medicine and Cardiology, Central Railway Headquarters Hospital, Byculla, Mumbai 400 027.

Ph : 022-23717246 (Hosp) 022-22624556 (R); Fax : 022-22651044; Mobile : 09821364565/09821638617; Email : sbgupta@vsnl.net; Website : www.iseindia.org