Original Article

Population based family history analysis of Brahmins in a small town in India for the prevalence of type-2 diabetes mellitus

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OBJECTIVES: The objective of this study is to determine the inheritance pattern of type-2 diabetes and make stratification for the general population risk.
MATERIALS AND METHODS: A questionnaire was developed for o btaining the family history. Analysis of the data was carried out by using student and Chi-square tests and for stratification; the guidelines of Scheuner *et al.* were followed.
RESULTS: The pattern of inheritance is the male sex specific (χ^2 =13.44). The mean age of onset of diabetes in parents was 58.61 ± 2.94 and in offspring 46.75 ± 2.54. In all 47.22 ± 11.53% families were found in high risk and 31.94 ± 10.77% in the moderate risk category. In female diabetics, the onset was in the age range of 41-60 years.
CONCLUSION: We found a high-risk of diabetes and familial clustering in successive generations of Brahmins with prominent male sex specificity. In females onset of diabetes was coinciding with the period around menopause.

Key words: Brahmin community, family history, inheritance pattern, risk stratification, type-2 diabetes

Introduction

Rahuri is a small town located on the banks of Mula River North of Ahmednagar city in the state of Maharashtra in India. It has latitude of 19°24' and longitude of 74°29'.

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There are 120-130 families belonging to the Brahmin caste in this town. It is a minority caste that is economically and socially advanced. The population size of this community is estimated to be 2500-3000.

Diabetes mellitus is a group of metabolic disorders with a partial or absolute insufficiency of insulin secretion and with various degrees of insulin resistance. The type-2 form of diabetes is one of the most common non-communicable diseases in the world. The so called diabetes epidemic is related to type-2 diabetes (non-insulin-dependent diabetes mellitus), which is spreading both in developed and developing nations.[1,2] Non-communicable diseases such as diabetes have become the serious public health challenge of this century due to its impact on individual and national health. The world-wide prevalence of diabetes is predicted to reach 4.4% in 2030 by the World Health Organization (WHO).[3] The WHO has predicted that India would experience the largest increase in prevalence of type-2 diabetes and would have the greatest number of a diabetic individuals living by the year 2030.

From a genetic perspective, the population of India is unique in size and level of diversity. It is multi-religious with a majority of the population following the Hindu religion. In this country, there are many castes sub-castes and further subdivisions in all religions. As a result, the Indian population is composed of many endogamous subpopulations. Naturally various genetic pools have been formed in the Indian society. The clinical consequences of such complex differentiation have been largely ignored.[4]

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Data on the prevalence of type-2 diabetes in India is very limited and very little information is available for the caste and sub-caste wise break up. Not only thiseven the data considering socio-economic, rural-urban and geographical disparity on the prevalence of type-2 diabetes is limited.[5]

Kumar *et al*.[6] have observed a high prevalence of type-2 diabetes in urban areas of Assam state of India. In South India, most of the studies are focused on the urban areas in cities such as Hyderabad and Chennai. However, recent studies have shown an increase in diabetes in peri-urban villages and rural areas in South India.[7,8] In Western India, majority of studies on the prevalence of type-2 diabetes have been conducted in Mumbai and Ahmedabad. The conclusion of all these studies is that there is an explosion of type-2 form of diabetes in India irrespective of rural or urban population even though the prevalence of diabetes in rural India is lower than the urban parts.[9] Recent studies carried out by Kothari *et al*.[10] have observed a very high prevalence of type-2 diabetes in the "Bhargava" sub-caste of the Brahmin population in India.

Family history is the most easy and relevant way of forecasting prevalence of diabetes. In fact, some studies have suggested that the contribution of family history could be an independent guide for assessing risk of the disease.[11-13]

Population based family history analysis for type-2 diabetes and its stratification as per the Scheuner *et al*. guidelines is important in India for differentiating susceptible castes and sub-castes for improving the health standard. The present analysis is on a sample data of 72 Brahmin families of the Rahuri town.

Materials and Methods

A core of set of questions was developed in the local language for collection of the family history for type-2 diabetes mellitus from the head of the family. In the questionnaire, maternal family history was also obtained since it is also a strong independent risk factor.[14]

A door-to-door approach was preferred for filling the questionnaire. The face-to-face interview with the family head made us easy to construct pedigrees including three generations and in some cases even four generations.

The questions were phrased precisely for obtaining the desired information. The reporting accuracy was confirmed from grandparents, aunts, uncles and other relatives for the validity. The medical reports, prescriptions, diagnosis, the age of onset etc., were also confirmed while filling the questionnaire. In short, the analytical validity of family history was increased by filtering much of the noise. Finally, the signature of the family head was taken at the end of the questionnaire confirming the authenticity of the information. The privacy of information was very strictly maintained for avoiding legal and social implications.

We were able to obtain the family history for type-2 diabetes from 76 families while 7 families refused to respond positively. Out of 76 families, the family history of 4 families were not complete enough to construct a pedigree and hence omitted from data analysis.

Finally, the family history of 72 families was used for constructing pedigrees and further analysis. Data were analyzed for (1) general population risk on the basis of suggested guidelines for risk stratification based on family history,[15] (2) pattern of inheritance, (3) susceptibility among either sex, (4) difference in the age of onset among parents and offspring and (5) incidence of type-2 diabetes among females by using Chi-square and *t*-tests.

Results and Discussion

In the population being analyzed, there were 140 males and 71 females with type-2 diabetes among 1136 individuals of 72 families [Table 1]. The families were classified according to Scheuner *et al*. guidelines [Table 2a]. This classification shows that people at high and moderate familial risk for type-2 diabetes were very common in the Brahmin population of this town.

As far as the age of onset of type-2 diabetes is concerned, we were able to obtain the age of onset of 54 affected existing females and 90 affected existing males. In females, the spectrum of age of onset is quite narrow and it falls in the age range of 31-60 years. On the other hand, the spectrum of the age of onset is

quite broad in males and falls within the age range of 21-80 years [Table 2b]. In females, most of the cases of onset of type-2 diabetes fall in the age range of 41-60 years. This age in females is a period around menopause. Higher percentage of onset of type-2 diabetes within this period among females cannot rule out the possibility of hormonal changes to be one of the factors in the process of diabetogenesis.

Table 1: Details of responders in the study

Description	Number
Total Brahmin families with complete family information	0072
Number of males in 72 families	0561
Number of females in 72 families	0575
Total individuals in 72 families	1136
Number of existing males with type-2 diabetes	0090
Number of affected but non-existing males	0050
Number of existing females with type-2 diabetes	0054
Number of affected but non-existing females	0017
Total existing individuals with type-2 diabetes	0144
Total affected but non-existing individuals	0067
Total number of existing+non-existing individuals with type-2 diabetes	0211

Table 2a: Stratification of Brahmin families for type-2 diabetes as per Scheuner's guidelines

Category	Total families	Percentage with standard error at 95% CI
High risk	34	47.22±11.53
Moderate risk	23	31.94±10.77
Average risk	15	20.83±9.38

CI: Confidence interval

Table 2b: Age of onset of type-2 diabetes in different class intervals of age in males and females

Class interval of age	Number of females	Percentage with SE at 95% CI	Number of males	Percentage with SE at 95% CI
21-30			02	2.22±4.73
31-40	14	25.92±11.69	13	14.44±7.26
41-50	23	42.59±13.19	21	23.33±8.74
51-60	17	31.48±12.39	40	44.44±10.27
61-70			12	13.33±7.02
71-80			02	2.22±4.73

CI: Confidence interval, SE: Standard error

Table 2c: Data showing χ^2 test of susceptibility and *P* values in offspring when both or either of the parents are diabetic

Status of parents	Number of diabetic off spring		χ^2 value and *P* value in bracket	Risk of inheritance in off spring
	Male	Female		
Both parents diabetic	08	05	0.6923 (0.4054)	Equal
Father diabetic	39	18	7.74 (0.0054)	Males at risk
Mother diabetic	13	03	6.25 (0.0124)	Males at risk
All diabetic parents	60	26	13.44 (0.0002)	Males at risk

For 1 df and 0.05 critical value, χ^2=3.841

Data analysis for the pattern of inheritance [Table 2c] shows equal risk of inheriting diabetes for male and female offspring when both parents are diabetic. However, sons are more affected when either of the parents is diabetic. From the same table, it is to be noted that diabetic sons were more likely to have a diabetic father – suggesting a male sex specific paternal inheritance. The *t*-test shows the mean parental age of onset of type-2 diabetes is 58.61 ± 2.94 and that in offspring 46.75 ± 2.54 in this population. Thus, there is a decrease in the age of onset when there was a parental history of type-2 diabetes. It indicates that the presence of diabetes in the family results in predisposition to diabetes in subsequent generations with clustering of different sets of genes, which could be responsible for type-2 diabetes in different families.

This study is limited and needs incorporation of information regarding other common chronic conditions within responders' pedigrees. Our next task is to collect the family histories for type-2 diabetes from different communities including other common chronic conditions and make a comparative study for understanding relations and severity. In India, genetics professionals are almost nil at district and rural levels. This is a very unfortunate situation, because is where the bulk of Indian population resides. Primary care physicians fail to recognize the importance of the family history for disease risk prediction and prevention. Majority of the physicians lack the knowledge of genetics if this situation were to be corrected, prevention and control of disease would be easier than it is today.

Conclusion

This study shows that in the Brahmin community high and moderate risk families are more with a tendency of familial clustering of genes in successive generations. Male sex specific susceptibility is very prominent and in female diabetics age of onset coincides with the period around menopause in most of the cases.

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