Familial Aggregation of Type 2 Diabetes Mellitus in Rural India

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Abstract: <u>Aim</u>: To evaluate familial transmission, age and sex distribution of type2 diabetes mellitus in rural population. <u>Materials and</u> <u>methods</u>: This is a cross-sectional study which was conducted among diabetic patients visiting NRIGH from January 2015 to June 2015. The study included patients diagnosed as T2DM as per WHO criteria [4] and attending regularly to medical OPD, taking oral hypoglycemic drugs. In this study, multistage stratified cluster sampling was employed using the administrative divisions of Tenali mandal. Of the 300 patients approached from different settlement areas of the mandal, 267 agreed to participate and gave verbal consent to take part in this study. <u>Results</u>: Patients above 30 yrs were taken in to study. Patients ranged from 30yrs to 85 yrs. Most patients were between age group 40 and 49 i.e. 80. Average age of onset of diabetes is 47.8 yrs. There was no much difference in gender ratio M:F =133:134. Out of 267 patients, family history of diabetes was evaluated and was present in 177 patients. The prevalence of DM in father, mother, brother and sister was 19.4%, 23.2%, 23% and 20% respectively. In 2nd degree relatives for uncles and aunts, a positive history of T2DM was more common among maternal aunts/uncles than in paternal aunts/uncles (31.0% vs 22.0%). Both maternal and paternal transmission of diabetes was present in 15 patients [5.6%]. <u>Conclusion</u>: In conclusion, the study findings showed an excess of maternal transmission of T2DM in rural India. The data support the dominant maternal role in the development of diabetes mellitus in their offspring.

Keywords: familial aggregation, type 2 diabetes, maternal transmission, rural india

1. Introduction

Diabetes a global public health problem associated with its devastating consequences has assumed epidemic proportion in developing countries of the world. The prevalence of diabetes for all the age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2003. The total number of persons with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030[1]. There is strong evidence that Indians have a greater degree of insulin-resistance and a stronger genetic predisposition to diabetes. As several of the factors associated with diabetes are potentially modifiable, this epidemic of diabetes can be curbed if proper measures are taken to increase physical activity and reduce obesity rates in adults and children[2]. In India the prevalence is 2.4% in rural population and 11.6% in urban population [3].

We conducted a study to find the association between heredity, and type-2 diabetes mellitus and its relation to onset of type - 2 diabetes mellitus.

Given the growing rate of diabetes and its far reaching societal and economic consequences, prevention of diabetes among people at high risk is a public health issue of clinical importance.

Diabetes is a disease that has a strong clustering in families and has a genetic component. It has been widely reported that the occurrence of T2DM is triggered by a genetic susceptibility and familial aggregation in several populations[3,4]. Family history is a well-known risk factor for the developing of T2DM. It was estimated that risk for diagnosed T2DM increases approximately two to four fold when one or both parents are affected[5]. Almost 25% to 33% of all T2DM patients have family members with diabetes. Having a first degree relative with the disease poses a 40% risk of developing diabetes[6]. T2DM patients are more likely to have diabetic mothers than diabetic fathers. The existence of excess maternal transmission of T2DM in offspring of affected mothers than affected fathers is currently debated[7]. Family history reflects both inherited genetic susceptibilities and shared environments which include cultural factors[8]. Thus, family history of diabetes may be a useful tool to identify individuals at increased risk of the disease and target behavior modifications that could potentially delay disease onset and improve health outcomes.

To the best of our knowledge, the patterns of familial transmission of T2DM in rural India have not been studied so far. This is the first cross-sectional survey of rural India to determine the influence of familial history of T2DM in the offspring.

2. Materials and Methods

This is a cross-sectional study, conducted among diabetic patients visiting NRIGH a hospital of NRI medical college from January 2015 to June 2015. The study included patients diagnosed with T2DM as per WHO criteria [4], and attending regularly to medical OPD who were taking oral hypoglycemic drugs. In this study, multistage stratified cluster sampling was employed using the administrative divisions of Tenali mandal. Target population of each settlement is approximately equal i.e 20. Stratification was done to obtain a representative sample of target population, with equal proportions from rural areas. Of the 300 patients approached from different settlement areas of the mandal, 267 agreed to participate and gave verbal consent to take part in this study.

Demographics

Tenali mandal is one of the 57 <u>mandals</u> in <u>Guntur district</u> of the <u>Indian</u> state of <u>Andhra Pradesh</u>. It is under the

administration of <u>Tenali revenue division</u> and the headquarters are located at <u>Tenali</u> city. The mandal is also a part of the <u>Andhra Pradesh Capital Region</u> under the jurisdiction of <u>APCRDA</u>.^[5]

As of 2011 <u>census</u>, the mandal had a population of 240,031. The total population constitute, 118,616 males and 121,415 females —a sex ratio of 1024 females per 1000 males. 21,333 children are in the age group of 0–6 years, of which 10,939 are boys and 10,394 are girls. The average literacy rate stands at 79.89% with 174,711 literates.

As of 2011 <u>census</u>, the mandal has 13 settlements. It includes 1 town and 12 villages. <u>Tenali</u> (M) is the most populated village and Nelapadu is the least populated village in the mandal.

The settlements in the mandal are listed below:

- 1. Angalakuduru
- 2. Burripalem
- 3. Chinaravuru (Rural)
- 4. Devarapalliseri
- 5. Gudivada
- 6. Katevaram
- 7. Kolakaluru
- 8. Nandivelugu
- 9. Nelapadu
- 10. Pedaravuru
- 11. Pinapadu (Rural)
- 12. Sangam Jagarlamudi



Inclusion criteria:

- 1. Patients above the age of 30 years.
- 2. Diagnosed as type 2 diabetes.

Exclusion criteria:

- 1.Patients with type 1 diabetes.
- 2. Patients who doesn't know his family history.

Questionnaire:

We developed a structured questionnaire consisting of questions relating to socio-demographic data, family history of diabetes mellitus (DM). The first part included information about socio-demographic characteristics, including age, sex and occupation. The second section collected information about family history of DM with family relations.

3. Observation and Results

In our study, total number of 267 patients were taken and questioned. There was no much difference in gender ratio. 133 were male, and 134 were female @ 49.8% and 50.2 % respectively. Fig 3.1 shows gender distribution.

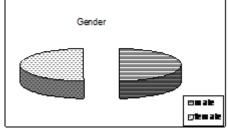


Figure 3.1: Gender distribution

Patients above 30 yrs were taken in to study. Patients ranged from 30yrs to 85 yrs. Most patients were between age group 40 and 49 i.e. 80. Average onset of diabetes is 47.8 yrs. Table 3.1 and Fig3.2shows age distribution of patients taken in to study. Table 3.1 - Age distribution

Age groups	
30- 39	20
40-49	80
50-59	78
60-69	65
70-79	18
Total	267

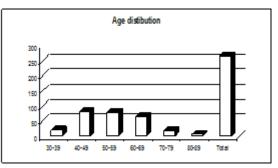


Figure 3.2: Age distribution

Family history of DM was significantly higher in female patients (51.4%). Family history of diabetes was more common in the age group 50 - 59 years.

Table 3.2 and Fig 3.3 reveal the familial history of diabetes mellitus among diabetic patients. Of the total study population, 66.29% reported a family history of DM. The prevalence of DM in father, mother, brother and sister was 19.4%, 23.2%, 23% and 20% respectively. In 2^{nd} degree relatives for uncles and aunts, a positive history of T2DM was more common among maternal aunts/uncles than in paternal aunts/uncles (31.0% *vs* 22.0%).

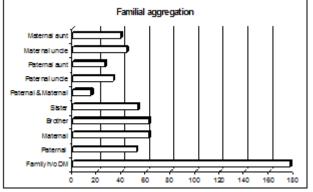


Figure 3.3: Familial aggregation

Table 3.2: familial aggregation of diabetes

	Number(n)	%
Family h/o DM	177	66.2
Father	52	19.4
Mother	62	23.2
Brother	62	23.2
Sister	53	20
Father and Mother	15	5.6
Paternal uncle	33	12.3
Paternal aunt	26	9.7
Maternal uncle	44	16.4
Maternal aunt	39	14.6

4. Discussion

Diabetes is the single most important metabolic disease, widely recognized as serious risk for target organ damage. In our study average onset of diabetes is 47.8 yrs had been noted which implies that these subjects develop diabetes in most productive years of their life and have a greater chance of developing complications. In developed countries, diabetes generally occurs in individuals aged > 65 yrs. In the developing countries onset of diabetes occurs at a younger age (45-65yrs)[3,30]. In studies from India, age of onset of diabetes is prevalent in much younger population compared to western population [31].Our study showed that the early onset of type -2 diabetes among patients having both parents with diabetic when compared to other patients. Ng et al[<u>14</u>] confirmed the similar findings in their study of a familial early onset of type-2 diabetes in Chinese patients

Ramachandran et al[5] observed similar findings in their study of parental influence on the spectrum of type 2 diabetes in the offspring among Indians. Familial clustering of type-2 diabetes is well-known and is high in Indians[6-8]. We found that, prevalence of diabetes was higher among patients with diabetic mother (23.2%) compared to patients with diabetic father (19.4%). Knowler et al[9] and Karter et al[10] observed similar findings in their study to assess diabetes incidence in Pima Indians and excess maternal transmission of type -2 diabetes respectively. The Framingham offspring study found that, maternal and paternal diabetes conferred equal risk for offspring type-2 diabetes, but offspring with maternal diabetes were at excess risk for exceeding sub diabetic glucose tolerance[11]. However, Vishwanathan et al[$\underline{6}$] and Alcolado et al[$\underline{12}$] found absence of excess maternal transmission of diabetes to the offspring, in contrast to our findings. Bo et al[13] conducted a study to note the on influence of a family history of diabetes on the clinical characteristics of patients with type- 2 diabetes mellitus and found that the prevalence of diabetes in mother, father, and other relatives was 25.5%, 6.54% and 21.2% respectively.

In rural India, as a result of changing lifestyle due to rapid urbanization, the prevalence of T2DM is increasing, as is observed worldwide. However, the role of genetic and environmental factors remains unclear. This is the first study to provide insight in the familial aggregation and transmission patterns of T2DM among rural India. The study sample revealed that 66.29% of the subjects with DM had a positive family history of diabetes among at least one of their parents, siblings, uncles, and aunts.

The degree of familial aggregation of diabetes among Qatar nationals[17] found that 72.9% of the diabetic patients had a positive family history of diabetes among at least one of their relatives from both sides, which is nearly identical to our study. The degree of familial aggregation of diabetes among Tunisians[17] found that 70% of the diabetic patients had a positive family history of diabetes among at least one of their relatives from both sides, which is nearly identical to our study. A lower rate was observed in a French study[3] in which 66% of the diabetic patients had at least one relative with diabetes among their first and second degree relatives. Similar higher frequencies have also been reported among South Indians[18] (53.9%) and Pakistanis (70%)[19]. On the other hand, lower frequencies of positive family history have been reported by other studies in Asians[4] (36%), Europeans[20] (33%) and black South Africans (27%)[3]. In the study sample of 1980 diabetic patients, 71% reported at least one first degree familial member, which is similar to the study results of Crispin et al [21] (76.6%). These results support the strong familial aggregation of diabetes among an Arab population with a high prevalence among 1st degree relatives. Also, these study findings have proven that people with a family history of diabetes consider themselves to be at greater risk of developing diabetes in their offspring. These results are in agreement with a study by Hariri et al[22] that a family history of diabetes in a first-degree relative doubles a person's risk of developing diabetes.

Another important study finding was that the investigation of parental transmission patterns of T2DM showed an excess of maternal transmission of T2DM as mothers were implicated more frequently than fathers[23]. In the study sample, 23.2% of the mothers of the diabetic patients were diabetic compared to 19.4% of the fathers. Consistent with our results, a higher frequency of positive family history among mothers than fathers was reported in studies conducted in Brazil[21] (48.4% vs 21.3%), Britain[23] (36% vs 15%), France[24] (33% vs 17%), Greece[25] (27.7% vs 11%) and Tunisia[17] (21% vs 10%).

The present study extends the scope of genetic influence on DM by including parents, siblings, uncles, and aunts in the familial history. The excess maternal transmission of T2DM reported in this study is in line with studies from different populations with varying frequencies[15,16,18,21,25]. A positive family history of T2DM was more common among maternal aunts/uncles (31%) than in paternal aunts/uncles (22%), showing that this maternal effect likely extends to the

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previous generation in 2^{nd} degree relatives, as reported in another study[21]. These study results support the existence of excess of maternal transmission of T2DM in their population. On the contrary, in the Framingham population study[26], maternal and paternal diabetes conferred equivalent risk for occurrence of T2DM in offspring. In contrast to these findings, McCarthy et al[27] found no difference in parental transmission of T2DM in a population with high prevalence of diabetes. Longer average life span in women could increase the likelihood that mothers develop T2DM. Fathers may have more undetected diabetes because of reduced screening rates and health care utilization or may develop diabetes at an older age than mothers.

Harrison et al[32] documented that family history information may serve as a useful tool for public health because it reflects both genetic and environmental factors. Examining family history of DM may be a valuable approach for identifying patients at risk for diabetes. In addition, this survey provides some indication that knowledge of family history of diabetes may lead to identifying people at increased risk of diabetes and perhaps motivate them to make preventive life style changes that could favorably affect both clinical practice and patient behavior.

In conclusion, the study findings showed an excess of maternal transmission of T2DM in rural india. The data support the dominant maternal role in the development of diabetes mellitus in their offspring. The presence of a family history of diabetes resulted in an early onset of the disease of the offspring. Interventions to change life style habits among families might reduce the risk of diabetes in the offspring of diabetic patients.

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