

Family History – An Indicator For Developing Type 2 Diabetes At Earlier Age

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Abstract

Objective: Positive family history is an indicator for developing diabetes. Data are needed to determine if it effects age at onset of diabetes.

Method: This cross-sectional study was conducted at Ghurki Trust Teaching Hospital (GTTH) Lahore, in Diabetic And General Medical OPD. Enrollment for study began on January 1st 2020, and ended on March 31st, 2020. We conducted a Cross-sectional study. 933 diabetics and 396 non diabetics were interviewed regarding family history and age at onset of diabetes. Patients were then categorized into three groups based on their familial risk as average, moderate and high.

Results: In the diabetic group 487 (52.2%) had an average familial risk of developing diabetes, while 299 (32%) and 147 (15.8%) had moderate and high familial risk respectively. Conversely, similar groups among the non-diabetic population had 312 (78.8%), 69 (17.4%) and 15 (3.8%) familial risk of developing diabetes. Relation of family history with the age at the time of diagnosis of diabetes was statistically significant ($P < 0.0001$). In average risk diabetes group the average age at time of diagnosis of DM was found to be 43.9 years, whereas, with average, moderate and high familial risk the average age of the onset of diabetes was 46.04, 41.70 and 41.28 years, respectively. The individuals with a family history of diabetes are 2.83 times (95% CI: 2.19-3.65) more likely to get diabetes as compared to those with no family history of diabetes. Females were found to be 1.6 times more likely to have an early onset of diabetes and there are 1.88 times (95% CI: 1.18-2.99) more chances of having diabetes if the mother is diabetic ($P < 0.05$).

Conclusions: Family history is a strong independent predictor of diabetes. Patients with moderate to high risk of diabetes develop diabetes at an earlier age. Diabetic mothers confers more risk of early development of diabetes than any other relative.

Key Words: Type 2 Diabetes, Family History, Age at diagnosis

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Introduction

Diabetes Mellitus is the current century's pandemic. Developing world including Pakistan, being most effected. Diabetes patient number is on the rise and is

diagnosed at an earlier age. Now more people are living with diabetes in their productive years. This translates into increased number of lost work days, more spendature on health and morbidity. Type 2 accounts for more than 90% of all cases of diabetes.¹ Guidelines for management of diabetes not only focus on early detection, life style modification as well as early intensive glycemc control to prevent or delay complications once diabetes has set in.² Early detection depends on identification of risk factors so as to implement strategies which may help in delaying the disease onset. This study evaluated the use of self-reported family history of diabetes as a potential, independent screening tool to identify people at risk for developing the disease. The association of

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age at onset of diabetes with the number of first or second-degree family members having diabetes was studied. Few studies globally, but none in Pakistan have compared the age of onset of diabetes and their relationship with diabetic relatives.

Materials and Methods

This cross-sectional study was conducted at Ghurki trust teaching hospital (GTTH) Lahore, in diabetic and general medical OPD. Enrollment for study began on January 1st, 2020, and ended on March 31st, 2020. A total of 1329 patients (933 cases and 396 controls) were included. Patients were considered to be diabetic based on ADA 2020 criteria.³ A parent, brother, sister, or child was considered as First Degree Relatives (FDR). A second-degree relative is someone who shares 25% of a person's genes. It includes uncles, aunts, nephews, nieces, grandparents, grandchildren, half-siblings, and double cousins and third-degree relatives constituted the extended family i.e. first cousins, great grandparents and great grandchildren. Lineage is the line of descendants of a particular ancestor. All type 2 diabetics who were previously or recently diagnosed and agreed to participate in the study and render the required information were included. Type 1 diabetics were excluded. Controls were selected from general medical OPD. They were not known diabetics and agreed to get blood sugar levels checked and to render the required information. After being selected, a survey form was filled by the patient or some helper. This included the number of family members with diabetes, relationship to the patient, and age of the patient at the onset of diabetes. Using the number and type of affected relatives, participants were classified into average, moderate, or high familial risk.⁴ High: At least 1) two first-degree relatives with diabetes from the same lineage; 2) one first- and two second-degree relatives with diabetes from the same lineage; or 3) three second-degree relatives with diabetes from the same lineage. Moderate: Only 1) one first- and one second-degree relative with diabetes from the same lineage; 2) one first-degree relative with diabetes; 3) either mother or father with diabetes, or 4) two second-degree relatives from the same lineage with diabetes. Average: Only 1) one second-degree relative with diabetes from one or both sides of the family; or no family history of diabetes. The data was processed using SPSS version 21 and STATA. The validity of family history as a screening tool was examined by calculating sensitivity, specificity, positive and negative predictive values.

Logistic regression analysis was applied with and without adjustment for risk factors and Odds ratio was calculated. Association of age at onset of diabetes was evaluated with the number of family members having the disease and the effect of any particular relation to the patient with age at onset of diabetes.

Results

Of the 1329 patients inquired regarding the status of diabetes, 933 had a self-reported diagnosis of diabetes whereas the other 396 (29.8%) were non-diabetics. The demographic and baseline characteristics in both groups are depicted in Table-1. Both sample populations were stratified according to their familial risk into average, moderate and high risk groups. In the diabetic patients group 487(52.2%) had an average familial risk of developing diabetes, while 299 (32%) and 147 (15.8%) had moderate and high familial risk respectively. Conversely, similar groups among the non-diabetic population had 312 (78.8%), 69(17.4%) and 15(3.8%) familial risk of diabetes. (Fig-1). The individuals with a family history of diabetes are 2.83 times (95% CI: 2.19-3.65) more likely to get diabetes as compared to those participants with no family history of diabetes (Prob> χ^2 <0.0001, R²=0.0423). When gender was taken into consideration, it was found that females are 1.6 times more likely to have an early onset of diabetes with high familial risk as compared to males however this difference was statistically non-significant. Logistic regression analysis was applied for the age at onset of diabetes with and without any adjustment for risk factors like age, gender, and family history. The average age at onset of diabetes was 43.90 years. The analysis showed that in patients with no or average risk, the age of onset of diabetes was 48.5 years (OR: 2.79, 95% CI:3.77-1.83), with moderate risk it was 41.90 years while it decreased to 41.28 years if familial risk was high (P<0.0001) (Table-2) . By using logistic regression analysis, odds ratio was calculated by keeping negative family history as reference. For this, two models were derived, Model-1 did not have any variable adjusted whereas, and the model-2 was adjusted by gender. Model 1 showed that the diabetic population of our sample was having higher familial risk than the non-diabetic population (OR: 2.63, 95% CI: 2.12-3.27, P<0.0001), while model 2 when adjusted for gender did not show any statistical significance (Table-3). Model 1: No adjustment for any variable; Model 2: adjusted with family history and gender. Prob> χ^2 : the probability of obtaining chi-square, OR: odds ratio, CI: confidence interval. Association between familial risk and relationships (mother, father,

brother, sister and other distant family members) were also estimated using multiple logistic regression. The results showed that there are 1.88 times (95% CI: 1.18-2.99) more chances of developing diabetes if the mother is diabetic (P<0.05) while in case of father having DM, chances of developing diabetes was doubled if CI was set at 90% while it had non-significant relationship if CI was set at 95%. Furthermore, if both parents are diabetics then there is 33.5% more chance of having diabetes in the next generation (P<0.05). On the other hand, if a brother(s) and sister(s) are having a history of diabetes then the likeliness of having diabetes would be 32.0% (CI 95%: 18.9%-54.0%) and 57.9% (95%

CI: 34.3%-97.6%) high, respectively (P<0.05). If all siblings are having diabetes then there is 19.0% higher chance of getting diabetes. On contrary, if any other relative does have a history of diabetes then there is a non-significant chance of getting diabetes. Moreover, if parents and siblings have diabetes then the percentage of getting diabetes is 58% higher than non-diabetic population (P<0.05). There are absolute chances of getting diabetes if parents, siblings, and children are diabetics (P<0.05). (Table-4)

Table 1: Demographics of the study population.

		Patients (n=1329)					
		Non-Diabetics (n=396)			Diabetics (n=933)		
		Familial Risk Stratification			Familial Risk Stratification		
		Average (n=312)	Moderate (n=69)	High (n=15)	Average (n=487)	Moderate (n=299)	High (n=147)
Gender	Female	241 (60.9)	47 (11.9)	8 (2.0)	340 (36.4)	211 (22.6)	101 (10.8)
	Male	71 (17.9)	22 (5.6)	7 (1.8)	147 (15.8)	88 (9.4)	46 (4.9)
Family History	No	286 (72.2)	-	-	447 (47.9)	-	-
	Yes	26 (6.6)	69 (17.4)	15 (3.8)	40 (4.3)	299 (32.0)	147 (15.8)
Age at presentation	<18	18 (4.5)	0 (0.0)	0 (0.0)	3 (0.3)	0 (0.0)	0 (0.0)
	18-34	111 (28.0)	37 (9.3)	9 (2.3)	22 (2.4)	27 (2.9)	13 (1.4)
	35-54	133 (33.6)	22 (5.6)	4 (1.0)	274 (29.4)	185 (19.8)	88 (9.4)
	>54	50 (12.6)	10 (2.5)	2 (0.5)	188 (20.2)	87 (9.3)	46 (4.9)
Age group at time of diagnosis	<18	-	-	-	4 (0.4)	1 (0.1)	0 (0.0)
	18-34	-	-	-	64 (6.9)	69 (7.4)	38 (4.1)
	35-54	-	-	-	298 (31.9)	190 (20.4)	95 (10.2)
	>54	-	-	-	121 (13.0)	39 (4.2)	14 (1.5)
Family members having diagnosis of diabetes	Mother	0 (0.0)	29 (74.4)	10 (25.6)	0 (0.0)	181 (63.7)	103 (36.3)
	Father	0 (0.0)	6 (60.0)	4 (40.0)	0 (0.0)	56 (53.3)	49 (46.7)
	Brother	0 (0.0)	26 (70.3)	11 (29.7)	0 (0.0)	46 (36.8)	79 (63.2)
	Sister	0 (0.0)	26 (81.3)	6 (18.8)	0 (0.0)	55 (35.9)	98 (64.1)
	Children	0 (0.0)	0 (0.0)	1 (100)	0 (0.0)	6 (27.3)	16 (72.7)
	Other relatives	26 (81.3)	0 (0.0)	6 (18.8)	39 (47.0)	0 (0.0)	44 (53.0)

Table 2: Age at Diagnosis of diabetes

Age at time of diagnosis years)	Overall (N=933)	Familial Risk Stratification			Odds Ratio (95% CI)
		Average (n=487)	Moderate (n=299)	High (n=147)	
	43.90 ± 11.30	46.04 ± 11.77	41.70 ± 10.10	41.28 ± 10.66	2.79 (95% CI: 3.77-1.83)
<18	5 (0.5)	4 (0.8)	1 (0.3)	0 (0.0)	
18-34	171 (18.3)	64 (13.1)	69 (23.1)	38 (25.9)	
35-54	583 (62.5)	298 (61.2)	190 (63.6)	95 (64.6)	
>55	174 (18.7)	121 (24.9)	39 (13.0)	14 (9.5)	
P<0.0001					

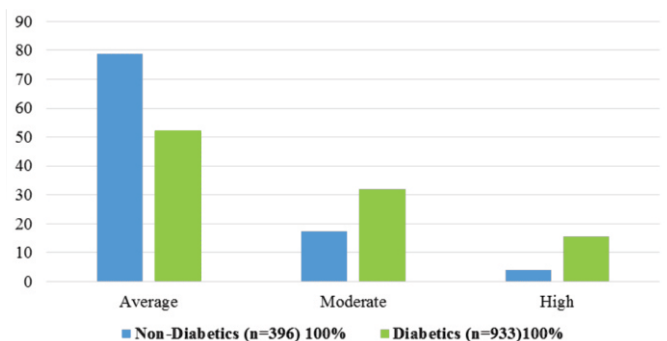


Fig-1: Distribution of risk according to family history

Table 3: Association between family history and risk of diabetes

	Prob> χ^2	Odds Ratio (OR)	95% CI	P-value
Model 1	<0.0001	2.63	2.12 – 3.27	<0.0001
Model 2	<0.0001	1.23	0.93 – 1.62	>0.05

Table 4: Association of relationship to patient with chances of getting diabetes

Relationship to patient	Chance of getting Diabetes	CI	P Value
Mother Alone	1.8 Times	95%	<0.05
Father Alone	-	95%	>0.05
Father Alone	2 Times	90%	<0.05
Mother + Father	33.5%	95%	<0.05
Brother	32%	95%	<0.05
Sister	57.9%	95%	<0.05
All Siblings	19.0%	95%	<0.05
Parents + Siblings	58%	95%	<0.05
Parents+Siblings+Children	100%	95%	<0.05
Other Relatives	-	95%	>0.05

Discussion

This study evaluated the use of self-reported family history of diabetes as a potential screening tool to identify people at risk for diabetes. The study showed that individuals with a family history of diabetes have a higher risk of developing diabetes as compared to the subjects with no family history and also at an earlier age.¹ Family history in fact is a stronger independent predictor of diabetes when compared to other anthropometric, genetic, and lifestyle factors.⁵ Although, this study did not take into consideration other anthropometric and genetic factors but did show that familial risk of diabetes is unaffected by gender stratification. Hence, the risk of type 2 diabetes is equally present in both genders. However, other biological and socioeconomic factors associated to each gender may result in higher familial

risk of diabetes.^{6,9} An early onset of diabetes is strongly associated with a high familial risk of diabetes. In cases with no or average risk of diabetes, the mean likely age of diabetes at time of diagnosis was found to be 46.04 years and decreased to 41.70 and 41.28 years respectively in patients with moderate and high risk of disease. Average age at diagnosis of diabetes was found to be 43.9 years whereas in another study by us in 2014 showed that average age at diagnosis was 44.1 years.¹⁰ This downward trend was observed in other studies too.^{5,11} The early onset of diabetes results in the impaired quality of life and early appearance of chronic complications giving rise to immense healthcare and economic burden. Therefore, family history may be used as an effective tool to ascertain the probability of occurrence of diabetes and may help in monitoring at earlier age and adopt life style modification at appropriate time. Study also showed that there is twice as much chance of developing type 2 diabetes if the mother is diabetic, while a weaker correlation is present if the father is diabetic^{12,13} again helping to adopt life style modification at earlier age. This might be due to the occurrence of maternal dysglycemia drastically affecting intra uterine environment during gestational diabetes hence, an elevated risk of diabetes is present in the child.^{5,14-16} Similarly, the likelihood of getting diabetes also relies upon siblings where we observed that the chances of diabetes are comparatively higher if the sister is diagnosed with diabetes as compared to brother. The exact mechanism of familial transmission of diabetes is still debatable though impaired secretion of insulin or resistance may be the mechanism involved.¹⁷⁻²⁰ The scope of our study was limited to assess the association of familial risk to predict type 2 diabetes mellitus. To our knowledge, this study was the first of its kind in Pakistani population and it concludes that family history is a strong independent predictor of diabetes. Patients with moderate to high risk of diabetes develop diabetes at an earlier age. Diabetic mothers confers more risk of early development of diabetes than any other relative. Family history may be employed as a valuable and inexpensive tool for the early detection of diabetes. This will help in early screening and adoption of healthy lifestyle including diet, exercise and weight control.

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None

Conflict of Interest

None

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Authors Contribution

WA, SS: Conceptualization of Project

SSQ: Data Collection

JZ, SSQ: Literature Search

SSQ, WA: Statistical Analysis

BMB, SSQ: Drafting, Revision

SS, WA, JZ: Writing of Manuscript