

Association Between Parental History of Type 2 Diabetes and Glycemic Control in Urban African Americans

Lucy Gong¹, Wen Hong Linda Kao, PhD^{1,2}, Frederick L. Brancati, MD^{1,2}, MHS, Marian Batts-Turner, MSN, RN, CDE², Tiffany L Gary, PhD^{1,2}

From the Departments of Epidemiology (1), and Medicine (2) The Johns Hopkins Medical Institutions, Baltimore, MD.

Corresponding author:

Tiffany L. Gary, PhD
Email: tgary@jhsph.edu

Running Head: *Family History & Glycemic Control*

Received 26 March 2008 and accepted 27 May 2008.

This is an uncopyedited electronic version of an article accepted for publication in *Diabetes Care*. The American Diabetes Association, publisher of *Diabetes Care*, is not responsible for any errors or omissions in this version of the manuscript or any version derived from it by third parties. The definitive publisher-authenticated version will be available in a future issue of *Diabetes Care* in print and online at <http://care.diabetesjournals.org>.

Objective: To examine the association between parental history of type 2 diabetes and glycemic control among diabetic urban African Americans.

Research Design and Methods: Study participants included 359 African Americans with type 2 diabetes from Baltimore City, Maryland enrolled in Project Sugar 2. Participants underwent an interview administered questionnaire that asked about family history, socio-demographics, clinical characteristics, and knowledge and perception of adequate glycemic control. Regression analysis was used to determine the association between parental history of diabetes and glycemic control, as measured by HbA1c.

Results: In the comparisons between participants with and without parental history of diabetes, those with positive parental history tended to be younger, have higher glucose levels, and higher blood sugar levels before calling a doctor (all $P < 0.05$). After adjusting for age, sex, and BMI, there was a significant association ($P = 0.02$) between HbA1c and parental history with the mean HbA1c difference between those with a positive and a negative parental history being 0.58 %. However, after adjusting for duration of diabetes, the association was no longer significant ($P = 0.11$). However, there was a tendency for individuals with two diabetic parents to have higher HbA1c ($P = 0.011$).

Conclusions: From these results, we conclude that among the urban African American participants who were aware of their parental history of diabetes, positive parental history was associated with worse glycemic control, partly due to longer duration of diabetes. Parental history did not appear to be associated with better knowledge or perception of adequate glycemic control.

Many studies have investigated risk factors for type 2 diabetes (1), for instance, it has been well established that family history of type 2 diabetes has been found to be associated with an increased risk of developing the disease (2,3). However, there are few studies evaluating the effects of family history on poor glycemic control, which has been found to be associated with many serious complications among individuals living with type 2 diabetes (4,5). Consequently, family history continues to be under utilized in disease prevention (6,7) and not often consulted after the initial disease diagnosis.

Family history could have effects on glycemic control via genetic or behavioral mechanisms. For example, individuals with diabetes who have a parental history of type 2 diabetes may have worse glycemic control, in part due to the genetic risk factors of the disease that may then influence the severity or duration of the condition. Alternatively, they could have better glycemic control, in part due to improved knowledge of the disease or health behaviors as a result of having affected family members. We conducted a study to quantify these effects and determine overall effect on glycemic control.

This study has important clinical practice implications. If glycemic control is associated with family history, it is possible that given a patient's family history, clinicians will have insight not only of the risk of developing type 2 diabetes but also of its severity.

METHODS

Study Population: The participants were 542 African-Americans from Baltimore City in Project Sugar 2, a randomized controlled trial to study the effects of nurse case manager and community health worker team interventions in improving diabetic control. Potential participants were identified

using an university-affiliated managed care organization (MCO) database and met the following criteria: ≥ 25 years of age, presence of type 2 diabetes (ICD-9 = 250), and no evidence of significant comorbid conditions likely to lead to death within the next 3-5 years (e.g. cancer, AIDS, end-stage renal disease, active tuberculosis, Alzheimer's disease, congestive heart failure). These potential participants were then screened by telephone to determine whether or not they met the study's eligibility criteria: African American by self report, Baltimore city resident, age 25 or older, receiving care at one of the six clinic sites, and no active participation in the MCO's other disease management programs. Other exclusion criteria was determined during the baseline screening visit: unable or unwilling to give informed consent, unable to complete baseline assessment (interview, clinical measures, venipuncture), or having a severe psychiatric health condition. Out of the 2,450 individuals who were screened, 542 agreed to enroll in the trial. Additional details of the recruitment process and characteristics of participants and nonparticipants can be found elsewhere (8). "The roughly 3 to 1 female-male ratio shown in our study was also noted in the non-participants, most likely reflecting that women with diabetes are more likely than men with diabetes to be enrolled in primary care."

For the present analysis, we excluded 183 individuals either because they were missing a measured Hemoglobin A1c (HbA1c) value ($n = 14$) or were unaware of their parental diabetes history ($n = 169$). This left us with 359 participants. When comparing the included and excluded individuals from the study, those included tended to be younger (56.2 compared to 60.2 years, $P < 0.001$) and have less education (15.9% vs 24.6% with $>$ high school education, $P = 0.005$). Other selected characteristics such

as sex, type 2 diabetes duration, BMI, glucose levels, A1C, and presence of hypertension (defined as having a systolic or diastolic blood pressure above or equal to 130 or 80 respectively) were not significantly different.

Family History of Diabetes: Family history was characterized through an interview administered questionnaire. Participants were asked about the medical histories of their biological mother and father, including details concerning whether they were alive or deceased and their diabetes status. We then grouped the individuals who knew their family history, depending on whether they had zero, one, or two parents affected with diabetes. In addition, we classified the individuals as having negative parental history, if both parents have never had diabetes, or positive parental history, if at least one parent has or had diabetes.

Glycemic Control: HbA1c, commonly abbreviated as A1C, is a general measure of diabetic control and an indicator of an individual's blood sugar control over the past 2-3 months (9). An A1C of <7% is a recommended aim for individuals with diabetes (9) with higher A1C corresponding to a higher mean plasma glucose level, indicating worse glycemic control (10). In this study, A1C was measured using venipuncture drawn blood samples and high-pressure liquid chromatography.

Confounders/Mediators: Potential confounders or mediators of the association between family history of diabetes and glycemic control, age, sex, duration of diabetes, and knowledge and perception of adequate glycemic control were determined by questionnaire. Body mass index (BMI) was calculated using measured height and weight.

Data Analysis: T-tests and chi-square tests were used to evaluate the differences in characteristics between the participants either included or excluded from this study. These

tests were also used to compare selected characteristics and perceptions of the included participants having a positive parental diabetic history with those included and having a negative history. Multiple linear regression models were used to determine the crude association between A1C and type 2 diabetes parental history with the beta-coefficients (β) representing the difference in mean A1C between having a negative and positive diabetic parental history. These models were then adjusted to account for potential confounders/mediators in stages. Stage 1: age, sex, Stage 2: +BMI, and Stage 3: + diabetes duration. All data analysis was completed using statistical software by STATA statistical software (College Station, TX) and significance was determined by an alpha level of 0.05.

RESULTS

Selected Characteristics of the Study Participants: Selected socio-demographic, behavioral and clinical characteristics of the 359 included study participants are shown in Table 1. The 150 participants with a negative parental history had a mean age of 59.2 years, which was significantly older than those 209 participants with a positive parental history (mean age of 53.9 years). Random (non-fasting) glucose levels were significantly higher in those participants with positive parental history ($P = 0.004$). Type 2 diabetes duration was slightly higher in those participants with a positive parental history, but that was not significantly significant. Both participants with a negative and positive parental history were predominantly female (24.7% male having negative parental history and 27.3% male having positive parental history). The majority of both groups had an education level between 8 to 12 years (no significant difference). These characteristics and others such as BMI, waist-to-hip ratio, cholesterol, high density lipoprotein cholesterol, hypertension, diastolic blood

pressure, and systolic blood pressure were not significantly different by parental history of diabetes.

Association between A1c and Parental History: In the box plot graph shown in Figure 1, individuals with affected parents tend to have significantly higher A1C (unadjusted $P = 0.011$). In addition, with an increasing number of affected parents, the mean A1C increased. After adjustment for age and sex, the relationship persisted. However, after further adjustment for duration of diabetes, the p-value became non-significant ($P=0.09$).

Linear regression models of the association between A1C and parental history are shown in Table 2. There was a strong significant association between A1c and parental history ($\beta = 0.67$ and $P = 0.006$). Even when adjusting for age, sex, and BMI, the association was still significant ($\beta = 0.58$ and $P = 0.02$). However, after considering duration of diabetes as a factor, this association was no longer significant, with a β coefficient value of 0.40 and P value of 0.11.

Knowledge and Perception of Adequate Glycemic Control: Of the 359 participants, 284 answered questions based on their knowledge and perception of glycemic control (Table 1). Individuals with positive parental diabetic history tended to report slightly higher blood sugar levels before calling a doctor (287.02 vs. 259.59 mg/dL, $P = 0.04$). Perception of perfect blood sugar levels did not significantly differ between those with negative or positive diabetic parental history.

DISCUSSION

Our findings point to several conclusions about this population of urban African Americans with type 2 diabetes. It is evident that a high proportion of urban African Americans are not completely aware of the diabetes statuses of their parents.

However, among those who knew their parental diabetic history, positive parental history of type 2 diabetes was associated with worse glycemic control, as indicated by longer duration of diabetes. This positive parental history of diabetes was not associated with better knowledge or perception of adequate glycemic control.

A strong association between A1c and parental history was shown, even when adjusting for age, sex, and BMI, indicating that these were not factors that significantly influenced the relationship. However, duration of diabetes caused the association to become no longer significant.

It is possible that the association between a positive parental history of diabetes and worse glycemic control is largely accounted for by parental history's association with longer diabetes duration. Therefore, the fact that urban African Americans with type 2 diabetes and a positive parental history of diabetes tend to have worse glycemic control may be related to developing diabetes at an earlier age, causing a longer duration of the condition. The age of an individual when he/she is diagnosed with the disease is an important factor in determining further family history risk (7).

Those with a positive parental history tended to report higher blood sugar levels before calling a doctor, which may indicate that they underestimate the seriousness of their diabetes (11). For instance, these individuals may be accustomed to seeing family members having higher blood sugar levels and may be less concerned about the severity of the disease than those who do not have as much family experience with diabetes. Also, we found that individuals with positive parental history have higher blood glucose levels, indicating that there may be differences in care and self-management.

The data also show that participants with negative family history tend to be older than those with a positive parental history.

This may be because older individuals are more likely to forget their parental history and those who were not aware of their parental history were classified as having a negative history. Another possibility may be that participants with a negative parental history tend to live longer. This is especially probable given the possibility that those with negative histories may have a less severe case of diabetes since they tend to have a slightly shorter duration of the disease and lower fasting glucose levels. Genetic risk factors may have contributed to the significantly higher glucose levels present in those with positive histories, giving these people more severe cases of diabetes.

Our study has several strengths. It is one of the first studies to investigate the association between parental history of type 2 diabetes and glycemic control among African Americans. While the association between parental history and the risk of diabetes has been well established (12), this study is unique as it relates parental history to glycemic control. This adds further evidence of genetics contributing not only to an diabetes incidence (13) but also to hyperglycemia (14) and increasing the severity of the disease. In addition, this study includes a large sample of urban African Americans and is clinic-based, indicating that the conclusions drawn here may be applicable to this population as a whole.

There are also a few limitations of this study. A large proportion of the participants were unable to provide parental history information. These individuals were then dropped from the study, decreasing the sample size. Even with the included participants, there is the possibility of family history misclassification. Finally, there is limited data on participants' health behaviors. From this study, we are unable to tell whether other health related actions influenced the association between parental history and glycemic control.

In this study, there is evidence of an association between parental history of type 2 diabetes and glycemic control in urban African Americans with diabetes. This finding can have important clinical implications in how clinicians use parental history in treating individuals with diabetes. Since the sample size of this study was small, larger datasets are needed to confirm this relationship.

ACKNOWLEDGMENTS

We would like to acknowledge the efforts of the *Project Sugar 2* research staff and the Johns Hopkins General Clinical Research Center (GCRC). We also acknowledge the *Project Sugar 2* participants whose cooperation made this research possible.

The project was funded by grants from the National Institutes of Health (R01-DK48117 and R00052). Dr. Gary was funded by a grant from the NHLBI (K01-HL084700) and Dr. Brancati was funded by a grant from the NIDDK (K24-DK6222).

The results were presented in part at the 63rd Scientific Sessions of the American Diabetes Association, New Orleans, LA, June 2003.

REFERENCES

1. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 26 Suppl 1:S5-20, 2003
2. Harrison TA, Hindorff LA, Kim H, Wines RC, Bowen DJ, McGrath BB, Edwards KL: Family history of diabetes as a potential public health tool. *Am J Prev Med* 24:152-159, 2003
3. Meigs JB, Cupples LA, Wilson PW: Parental transmission of type 2 diabetes: the Framingham Offspring Study. *Diabetes* 49:2201-2207, 2000
4. Gaster B, Hirsch IB: The effects of improved glycemic control on complications in type 2 diabetes. *Arch Intern Med* 158:134-140, 1998
5. Klein R, Klein BE, Moss SE: Relation of glycemic control to diabetic microvascular complications in diabetes mellitus. *Ann Intern Med* 124:90-96, 1996
6. Yoon PW, Scheuner MT, Peterson-Oehlke KL, Gwinn M, Faucett A, Khoury MJ: Can family history be used as a tool for public health and preventive medicine? *Genet Med* 4:304-310, 2002
7. Yoon PW, Scheuner MT, Khoury MJ: Research priorities for evaluating family history in the prevention of common chronic diseases. *Am J Prev Med* 24:128-135, 2003
8. Gary TL, Batts-Turner M, Bone LR, Yeh HC, Wang NY, Hill-Briggs F, Levine DM, Powe NR, Hill MN, Saudek C, McGuire M, Brancati FL: A randomized controlled trial of the effects of nurse case manager and community health worker team interventions in urban African-Americans with type 2 diabetes. *Control Clin Trials* 25:53-66, 2004
9. Standards of medical care in diabetes. *Diabetes Care* 27 Suppl 1:S15-S35, 2004
10. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan D, Peterson CM, Sacks DB: Tests of glycemia in diabetes. *Diabetes Care* 27:1761-1773, 2004
11. Pierce M, Harding D, Ridout D, Keen H, Bradley C: Risk and prevention of type II diabetes: offspring's views. *Br J Gen Pract* 51:194-199, 2001
12. Klein BE, Klein R, Moss SE, Cruickshanks KJ: Parental history of diabetes in a population-based study. *Diabetes Care* 19:827-830, 1996
13. Busch CP, Hegele RA: Genetic determinants of type 2 diabetes mellitus. *Clin Genet* 60:243-254, 2001
14. Pearson ER, Starkey BJ, Powell RJ, Gribble FM, Clark PM, Hattersley AT: Genetic cause of hyperglycaemia and response to treatment in diabetes. *Lancet* 362:1275-1281, 2003

Table 1. Selected Characteristics of Diabetes of 359 Project Sugar 2 Participants by Parental History of Diabetes Mellitus

	Negative Parental History (n=150)	Positive Parental History (n=209)	P value
Age (yr)	59.2 (11.1)	53.9 (10.6)	<0.001
Sex (% male)	24.7	27.3	0.58
Education			
> 8 years	4.7	4.3	
8 – 12 years	74.7	67.9	0.31
> 12 years	20.7	27.8	
T2DM duration (yr)	7.2 (7.5)	8.7 (8.6)	0.10
Blood Glucose (mg/dl)	142.0 (69.4)	166.3 (85.1)	0.004
BMI (kg/m ²)	34.0 (8.0)	34.8 (9.0)	0.35
Waist-to-hip ratio	0.90 (0.06)	0.90 (0.07)	0.65
Cholesterol (mg/dl)	188.7 (38.2)	191.7 (52.6)	0.56
HDL cholesterol (mg/dl)	52.9 (15.4)	50.5 (14.7)	0.14
Hypertension (% yes)	74.0	70.3	0.45
Diastolic BP (mmHg)	78 (10.4)	80 (11.9)	0.14
Systolic BP (mmHg)	137 (20.6)	136 (20.8)	0.53
What is your level of perfect blood sugar (mg/dl)?*	122.9 (33.8)	125.0 (35.7)	0.60
How high would your blood sugar have to be before you called your doctor (mg/dl)?*	259.6 (115.8)	287.0 (108.2)	0.04

* N=284; 116 negative parental hx, 168 positive parental hx

Table 2. Linear Regression Models of the Crude and Adjusted Association between HbA1c and Parental History of Diabetes Mellitus in 359 Project Sugar 2 Participants

	β -coefficient (se)	P value
Unadjusted model	0.67 (0.24)	0.006
Adjusted for age and sex	0.56 (0.25)	0.02
+ BMI	0.58 (0.25)	0.02
+ type 2 diabetes duration	0.40 (0.25)	0.11

Figure 1. HbA1c by Parental History of Diabetes Mellitus in 359 Participants in Project Sugar 2

