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The Development of Type 2 Diabetes Among Hispanic Women With a Pregnancy Complicated by Gestational Diabetes

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Purpose: *Hispanic women who have had a pregnancy affected by gestational diabetes are at higher risk for subsequently developing type 2 diabetes. We assessed the incidence and risk factors for diabetes in this population.*

Methods: *Ninety women with a pregnancy complicated by gestational diabetes and receiving follow-up care at the Yakima Valley Farm Workers Clinics in Eastern Washington State between October 15, 1994 and February 15, 2001, were identified. Cox proportional hazard analysis was performed, comparing the rate of developing type 2 diabetes ($n = 14$) among those exposed and unexposed to various risk factors of interest. Known predictors for the development of type 2 diabetes were analyzed, and a cumulative hazard estimate was generated.*

Results: *At 3-year follow-up, there was a 14% cumulative incidence of type 2 diabetes among women with at least 1 prior gestational diabetes pregnancy. Women who had had at least 2 gestational diabetes pregnancies had a 2.5-fold increased risk (95% confidence interval 1.10, 5.79) of developing type 2 diabetes, compared with women with 1 gestational diabetes pregnancy.*

Conclusions: *The incidence of type 2 diabetes after a gestational diabetes pregnancy was approximately 5% per year in this entirely Hispanic population of rural farm-working families.*

Key Words: *Gestational diabetes, prevention, Hispanic women.*

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Type 2 diabetes mellitus (DM), also known as adult-onset diabetes, affects 2% to 3% of the adult population.[1] It is estimated that 2% to 5% of pregnant women in the United States develop gestational diabetes mellitus (GDM).[2] In those women with a history of gestational diabetes, the development of type 2 diabetes is most common in individuals over age 30[3,4] who weigh more than 120% of ideal body weight[4-10] and have a family history of diabetes.[11,12] Hispanic women have a 3-fold increased risk for developing type 2 diabetes, as compared with white women,[13] and a single study has shown that this risk is even greater in women with a history of gestational diabetes.[14] This finding has not been repeated.

It is now well established that early interventions in individuals with recent onset of diabetes can greatly diminish the morbidity and mortality associated with complications from systemic disease.[15,16] Programs designed to tighten glucose control and screen for renal, ocular, neurologic, and cardiovascular manifestations of the disease have been quite successful (E. Wagner, verbal communication, January 2000). Therefore, identification of individuals at risk for adult-onset diabetes and institution of appropriate, cost-effective screening of these individuals is supported.[17]

As the first step toward instituting a screening and prevention program in a presumed high-risk population, we assessed the incidence and risk factors for diabetes in Latina women with a history of a pregnancy complicated by gestational diabetes.

Methods

University of Washington Human Subjects Approval was obtained. Hispanic women with a pregnancy complicated by gestational diabetes and receiving care at the Yakima Valley Farm Workers Clinics (YVFWC) in Eastern Washington between October 15, 1994 and February 15, 2000, were identified by computerized diagnostic codes (n = 123). A diagnosis of GDM, defined as fasting blood glucose ≥ 200 mg/dL or abnormal 3-hour 50-g glucose tolerance test,[18] were verified at chart review in 93 women. Three women were found to be ineligible for study because there was no follow-up information available, or they did not have a pregnancy complicated by gestational diabetes during the study time period.

Information obtained from the records included date of birth, ethnicity, reference date (date of gestational diabetes pregnancy delivery), newborn weight, gestation at delivery, gravity, parity, education, employment, marital status, family history of diabetes (defined as at least 1 first-degree relative with DM or 2 second-degree relatives with DM), total number of pregnancies with GDM, first-trimester body mass index (BMI), history of hypertension, dates and number of clinic visits since reference date, types of visits, whether any screening was performed for DM, and whether conversion to type 2 DM had occurred during follow-up. Type 2 DM was defined as fasting blood glucose ≥ 126 mg/dL or blood glucose 2 hours after 75-g oral glucose load of ≥ 200 mg/dL or 2 random blood glucose values > 200 mg/dL.[18] These values were all obtained at least 8 weeks after delivery, on or before the end of follow-up (February 1, 2001). Also noted was type of treatment for type 2 DM (diet, oral medications, or insulin).

Continuous variables were evaluated in linear fashion, as well as by categoric analyses with biologically meaningful cutoffs. For example, it has been suggested that the development of type 2 DM is associated with age greater than 30 years at onset; therefore, age was analyzed in continuous fashion and also as a dichotomous variable (age < 30 years and age ≥ 30 years). BMI, parity, gestational weight, and gestational age were also analyzed as continuous and categoric variables.

Characteristics of women who converted to type 2 DM (n = 14) were compared with those that did not (n = 76). The association between conversion to type 2 DM and potential or known risk factors was assessed with univariate Cox proportional hazard analysis. This statistical method controls for the staggered entry and exit times during the study period, and therefore the at-risk time intervals for developing type 2 DM are individually defined for each subject. Time of entry and analysis origin were defined as the date of delivery of the gestational diabetes reference pregnancy plus 60 days. Time of exit was defined as date of failure or diagnosis of type 2 DM, the last date seen in clinic, or completion of the study on February 1, 2001. Follow-up included 75% of the cohort at 1.6 years, 50% at 2.3 years, and 25% at 3.6 years.

Multivariate Cox proportional hazard models[19] were constructed by using known a priori risk factors for the development of type 2 DM. Relative risks and 95% confidence intervals (CIs) were cal-

culated, comparing the risk of type 2 DM by levels of each risk factor in the model. A Nelson-Aalen cumulative hazard curve was generated. Statistical analyses were performed by using STATA software version 6.0 for personal computer (College Station, TX).

Results

Latina women delivering a baby between October 15, 1994 and February 15, 2000, whose pregnancy was complicated by GDM subsequently developed type 2 DM by February 15, 2001, at an overall rate of 15.6%, (14/90) (not adjusted for staggered entry and exit from the study). Nelson-Aalen cumulative hazard curve, shown in Fig 1, shows that at 1-year of follow-up, approximately 10% of the women had developed type 2 DM with over 80% of the cohort still available for follow-up. At 2-year follow-up, there was a cumulative incidence of type 2 DM of 14%, and over 50% of the cohort was still available for follow-up. At 3.6 years, 20% of the women had developed type 2 DM, but only 25% of the cohort remained for analysis. Beyond 3.6 years, rates become unreliable because less than 25% of the total cohort is represented in the risk set.

The characteristics of the women in the study are shown in Table 1. Women who developed type 2 DM were more likely to be older at time of exit from study, to have had at least 2 pregnancies complicated by GDM, to have a BMI > 30 kg/m^2, a family history of DM, or hypertension.

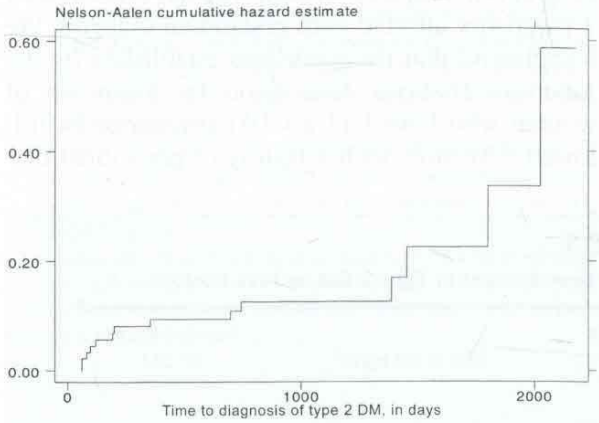

FIGURE 1. Cumulative incidence rates of type 2 DM as determined by Nelson-Aalen cumulative hazard estimate in 90 Latina women with prior GDM.

TABLE 1
Subject Characteristics

	Type 2 DM Conversion n/14 (%)	Nonconversion n/76 (%)
Age at exit (mean years)	34.1 (19.0-48.4)	32.9 (26.6-41.4)
Gravity	4.4 (range 2-10)	4.4 (range 1-17)
Parity	3.1 (range 1-9)	2.7 (range 0-12)
Married	10 (71.4)	55 (70.5)
Employed	4 (28.6)	22 (28.2)
Education > 12 years	3 (21.4)	18 (23.7)
≥2 GDM pregnancies	4 (28.6)	13 (16.0)
BMI ≥ 30 kg/m2	5 (38.5)	18 (23.7)
Family history of DM	9 (64.3)	35 (44.9)
Hypertension	4 (28.6)	10 (12.8)

Women who had had at least 2 pregnancies complicated by GDM had a 2.5-fold increased risk of developing type 2 DM, (95% CI 1.10, 5.79). Univariate analysis of selected potential risk factors for type 2 DM is shown in Table 2. Increased risks of developing type 2 DM were associated with BMI ≥ 30 kg/m^2, hypertension, a reference GDM twin gestation, and family history of DM; however, these were not statistically significant. All other variables tested did not show any association with the development of type 2 DM, including newborn weight, gestation at delivery, gravity, education, employment, marital status, dates and number of clinic visits since reference date, types of visits, and whether any screening was performed for DM.

TABLE 2
Univariate Proportional Hazard Risks and 95% CIs for Development of Type 2 DM by Risk Factors

Risk Factor	HR (95% CI)	*P*
Age ≥ 30 years (reference <30 years)	1.08 (0.36-3.26)	.87
Parity	1.07 (0.85-1.35)	.57
BMI ≥ 30 kg/m^2 (reference <30)	2.59 (0.71-9.49)	.15
≥2 GDM pregnancies	2.53 (1.10-5.79)	.03
Hypertension	2.13 (0.66-6.85)	.23
Reference twin gestation	6.02 (0.76-47.9)	.09
Family history of DM	2.14 (0.71-6.48)	.18

Abbreviation: HR, Hazard risk.

The relationships of known risk factors for the development of type 2 DM were explored in a multivariate Cox proportional hazard analysis as shown in Table 3. No adjustment was made for age, number of clinic visits, or number of screens performed for DM because these variables were not found to change the proportional hazard ratio by more than 10% on univariate analysis. As expected, the only significant risk factor was more than 2 pregnancies affected by GDM (including reference pregnancies) (Table 3, Model 1).

Discussion

The annual incidence rate of type 2 diabetes after a pregnancy complicated by gestational diabetes was found to be approximately 5% in this entirely Hispanic population of rural farm-working families. This rate of conversion to type 2 DM was half of that observed by Kjos and coworkers[14,20] in women of Mexican descent, living in the Los Angeles area. The Los Angeles group followed a larger cohort (n = 671). As in our study, women were only included if they did not have type 2 DM at the 4- to16-week postpartum visit. The percentage of subjects remaining in the Los Angeles cohort at various follow-up intervals was not described. Follow-up was defined as at least 1 75-g oral glucose tolerance test within 7.5 years. The percentage of the cohort followed beyond each year is not defined; therefore, as in our study, beyond 3.6 years the estimates of cumulative incidence rates may be artificially inflated because of low numbers in the risk sets. This cannot be directly ascertained from their report, but most likely beyond 4 years of follow-up, as estimated from the cumulative incidence rate figure given in their Fig 1, the numbers of individuals in the risk-sets diminishes appreciably.

We developed models to explore potential predictive risk factors for the development of type 2 DM. Risk factors with 2- to 3-fold elevated relative risks included at least 2 pregnancies complicated by GDM, nonpregnant BMI > 30 kg/m^2, hypertension, and a family history of DM. Despite a small sample size and concomitantly low power and wide CIs, these associations corroborate findings by the Los Angeles group.[14,20] Other investigators have shown an association between the development of type 2 DM in non-Hispanic mixed male and female populations without a history of GDM with elevated BMI, hypertension, and a family history of DM.[11,12] As in our study, Kjos and colleagues[14,20] did not find age or parity to be independent risk factors for development of type 2 DM in women with a history of GDM. Kjos and colleagues analyzed the area under the 3-hour oral glucose tolerance curve, the gestational age at time of diagnosis of GDM, and the highest fasting serum glucose concentration during pregnancy and found these to be strong predictors for later development of type 2 DM. The strongest predictor was the area under the 3-hour oral glucose tolerance curve for the postpartum glucose tolerance test. The highest quartile of this variable had a 5-year diabetes risk of 84%. As previously discussed, the percentage of the cohort remaining in the analysis at 5 years was not shown.[14]

In our study, the risk of type 2 DM associated with a twin gestational diabetic pregnancy was elevated 6-fold, but the CI was wide and spanning one. An association of twin pregnancy with GDM and the development of type 2 DM have not been previously described.

Our findings support an increase in the allocation of funds for diabetes screening and prevention programs in Hispanic women who have had at least 1 pregnancy affected with gestational diabetes. We recommend that the guidelines established by the American Diabetes Association for follow-up of women who have had a GDM pregnancy be followed.[18] Women with a history of gestational dia-

TABLE 3

Multivariate Proportional Hazard Risks and 95% CIs for Development of Type 2 DM by Risk Factors

	≥2 GDM Pregnancies	Reference Twin Gestation	BMI ≥ 30 kg/m^2	Family History of DM
Model 1	2.53 (1.10-5.79)			
Model 2	2.36 (0.98-5.70)	3.23 (0.34-27.15)		
Model 3	2.43 (0.99-5.98)	2.82 (0.32-24.31)	2.17 (0.58-8.19)	
Model 4	2.45 (0.96-6.26)	3.35 (0.37-30.42)	1.96 (0.51-7.48)	1.69 (0.53-5.38)

betes, and especially the high-risk population described in this study, should receive fasting blood glucose analysis and a 75-g glucose challenge with 2-hour post-challenge blood draw performed 6 to 8 weeks after delivery. Fasting ≥ 126 mg/dL or 2-hour post-challenge blood glucose of ≥ 200 mg/dL are considered abnormal, and women with these values should be referred for type 2 DM management. If the test is normal, yearly fasting blood glucose should be obtained. Values ≥ 126 mg/dL are abnormal. Although diet and exercise are important, seemingly simple preventative measures, they are sometimes the hardest to implement. A behavior modification project targeted at this high-risk population would be a valid use of resources.[21-23]

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References

1. National Diabetes Data Group: Diabetes in America (ed 2). Bethesda, MD, National Institutes of Health, 1995
2. Magee MS, Walden CE, Benedetti TJ, et al: Influence of diagnostic criteria on the incidence of gestational diabetes and perinatal morbidity. JAMA 269:609-615, 1993
3. Harris MI: Prevalence of noninsulin-dependent diabetes and impaired glucose tolerance, in Harris MI, Hamman RF, (eds): Diabetes in Amrerica. Washington, DC, U.S. Government Printing Office, 1985, DHHS publication # 85-1468: VI-1-VI-37
4. Stern MP: Diabetes in Hispanic Americans, in Harris MI, Hamman RF (eds): Diabetes in America. Washington D.C. U.S. Government Printing Office, 1985, DHHS publication # 85-1468:IX-1-IX-11
5. Metzger BE, Cho NH, Roston SM, et al: Prepregnancy weight and antepartum insulin secretion predict glucose tolerance five years after gestational diabetes mellitus. Diabetes Care 16:1598-1605, 1993
6. Cocilovo G, Tomasi F, Guerra S, et al: Risk factors associated with persistence of glucose intolerance one year after gestational diabetes. Diabet Metab 16:187-190, 1990
7. Catalano PM, Vargo KM, Bernstein IM, et al: Incidence and risk factors associated with abnormal glucose tolerance in women with gestational diabetes. Am J Obstet Gynecol 165:914-919, 1991
8. Coustan DR, Carpenter MW, O'Sullivan PS, et al: Gestational diabetes: predictors of subsequent disordered glucose metabolism. Am J Obstet Gynecol 168:1139-1145, 1993
9. O'Sullivan JB: Body weight and subsequent diabetes. JAMA 248:949-952, 1982
10. Persson B, Hanson U, Hartling SG, et al: Follow-up of women with previous GDM: Insulin C-peptide and proinsulin responses to oral glucose load. Diabetes 40:136-141, 1991 (suppl)
11. Martin BC, Warren JH, Krolweski AS, et al: Role of glucose and insulin resistance in the development of type 2 diabetes mellitus: Results of a 25-year follow-up study. Lancet 340: 925-929, 1992
12. Lo SS, Tun RY, Hawa M, Leslie RDG: Studies of diabetic twins. Diabetes Metab Rev 7:223-238, 1991
13. Haffner SM, Stern MP, Mitchell BD, et al: Incidence of type II diabetes in Mexican-Americans predicted by fasting insulin and glucose levels, obesity, and body-fat distribution. Diabetes 39:283-288, 1990
14. Kjos SL, Peters RK, Xiang A, et al: Predicting future diabetes in Latino women with gestational diabetes: Utility of early postpartum glucose tolerance testing. Diabetes 44:586-591, 1995
15. Nathan DM: Long term complications of diabetes mellitus. N Engl J Med 328:1676-1685, 1993
16. Clark CM, Lee DA: Prevention and treatment of the complications of diabetes mellitus. N Engl J Med 332:1210-1217, 1995
17. Vijan S, Stevens DL, Herman WH, et al: Screening, prevention, counseling, and treatment for the complications of type II diabetes mellitus, putting evidence into practice. J Gen Intern Med 12:567-580, 1997
18. Metzger BE, Coustan DR, the Organizing Committee: Summary and recommendations of the fourth international workshop conference on gestational diabetes. Diabetes Care 21:S60-S61, 1998
19. Breslow N: Covariance analysis of censored survival data. Biometrics 30:89-99, 1974
20. Kjos SL, Peters RK, Xiang A, Thomas D, et al: Contraception and the risk of type I diabetes mellitus in Latina women with prior gestational diabetes mellitus. JAMA 280:533-538, 1998
21. Okuson IS: Ethnic differences in the risk of type 2 diabetes attributable to differences in abdominal adiposity in American women. J Cardiovasc Risk 7:425-430, 2000
22. Eyler AA, Baker E, Cromer L, et al: Physical activity and minority women: a qualitative study. Health Educ Behav 25:640-652, 1998
23. The Diabetes Prevention Program Research Group: The Diabetes Prevention Program: Baseline characteristics of the randomized cohort. Diabetes Care 23:1619-1629, 2000