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Trends and Racial and Ethnic Disparities in the Prevalence of Pregestational Type 1 and Type 2 Diabetes in Northern California: 1996–2014

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Abstract

Background—Despite concern for adverse perinatal outcomes in women with diabetes prior to pregnancy, recent data on the prevalence of pregestational type 1 and type 2 diabetes in the U.S. are lacking.

Objective—To estimate changes in the prevalence of overall pregestational diabetes (all types) and pregestational type 1 and type 2 diabetes, and whether changes varied by race-ethnicity between 1996 and 2014.

Study design—Cohort study conducted among 655,428 pregnancies at a Northern California integrated health delivery system in 1996–2014. Logistic regression analyses provided estimates of prevalence and trends.

Results—The age-adjusted prevalence (per 100 deliveries) of overall pregestational diabetes increased from 1996–1999 to 2012–2014 (from 0.58 [95% CI 0.54, 0.63] to 1.06 [1.00, 1.12], $P_{\text{trend}} < 0.0001$). Significant increases occurred in all racial-ethnic groups; the largest relative increase was among Hispanic women (121.8% [84.4, 166.7]), while the smallest relative increase was among non-Hispanic White women (49.6% [27.5, 75.4]). The age-adjusted prevalence of pregestational type 1 and type 2 diabetes increased (from 0.14 [0.12, 0.16] to 0.23 [0.21, 0.27], $P_{\text{trend}} < .0001$, and from 0.42 [0.38, 0.46] to 0.78 [0.73, 0.83], $P_{\text{trend}} < .0001$, respectively). The greatest relative increase in the prevalence of type 1 diabetes was in non-Hispanic White (118.4%

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[70.0, 180.5]), who had the lowest increases in the prevalence of type 2 diabetes (13.6% [−8.0, 40.1]). The greatest relative increase in the prevalence of type 2 diabetes was in Hispanic (125.2% [84.8, 174.4]), followed by African American (102.0% [38.3, 194.3]) and Asian (93.3% [48.9, 150.9]).

Conclusions—The prevalence of overall pregestational diabetes and pregestational type 1 and type 2 diabetes increased from 1996–1999 to 2012–2014 and racial-ethnic disparities were observed, possibly due to differing prevalence of maternal obesity. Targeted prevention efforts, preconception care, and disease management strategies are needed to reduce the burden of diabetes and its sequelae.

Keywords

Diabetes; Pregnancy; Prevalence; Racial-ethnic Disparities

INTRODUCTION

Data on trends in the prevalence of pregestational diabetes and whether trends in the prevalence of pregestational type 1 and type 2 diabetes vary by race-ethnicity in the United States are needed. It has been reported that the predicted increases in the number of youth living with type 1 and type 2 diabetes by the year 2050 will be primarily among youth of minority racial-ethnic groups,¹ thus a similar racial-ethnic disparity in the prevalence of pregestational type 1 and type 2 diabetes might be expected. Three reports suggest that the prevalence of pregestational diabetes increased among pregnant women in the United States up to 2010.^{2–4} The only study that reported on trends in the prevalence of pregestational type 1 and type 2 diabetes did not include racial-ethnic specific prevalence estimates, and data were limited to 2004.³ Therefore, it is unknown whether increases in the prevalence of pregestational type 1 and type 2 diabetes vary by race-ethnicity.

Pregestational diabetes is associated with an increased risk of adverse perinatal outcomes, including preeclampsia,^{5, 6} retinopathy,⁷ early fetal loss,^{8, 9} stillbirth,¹⁰ macrosomia,¹¹ birth injuries associated with large fetal size, and infant death.^{10, 12} Given the burden of type 1 and type 2 diabetes during pregnancy, and recent changes in the racial-ethnic composition of women of reproductive age in the United States, understanding changes in the prevalence of pregestational diabetes, overall and by population subgroups, is important for informing health systems and clinicians of the resources required for the preconception and obstetric care of young women with diabetes.

The objective of this study was to estimate trends in the prevalence of overall pregestational diabetes (i.e., all types), as well as pregestational type 1 and type 2 diabetes (here after referred to as type 1 and type 2 diabetes), between 1996 and 2014, and examine whether changes in prevalence vary by race-ethnicity.

MATERIALS and METHODS

The study setting is Kaiser Permanente Northern California (KPNC), a large integrated healthcare delivery system consisting of 44 medical centers and 13 delivery hospitals

providing health care for approximately 33,000 deliveries per year. Analysis of U.S. census data demonstrates that KPNC members are representative of the geographic region served with regards to race-ethnicity and education, and differ only slightly at the extremes of the income distribution.^{13, 14} Women use the same KPNC medical center for general medicine and obstetrical care, including all laboratory testing. KPNC maintains complete databases of all hospitalizations, outpatient visits, laboratory tests, and medications dispensed through an electronic health record (EHR) system, in addition to housing a Diabetes Registry^{15, 16} and a Pregnancy Glucose Tolerance and Gestational Diabetes Registry.¹⁷ All laboratory tests performed during and outside of pregnancy are determined at a single location, the KPNC Regional Laboratory, which participates in the College of American Pathologists' accreditation and monitoring program.

This cohort study was conducted among pregnancies delivering at 20 weeks gestation between January 1, 1996 and December 31, 2014. Deliveries were identified by a method previously described.¹⁷ Clinically recognized diabetes prior to a pregnancy (i.e., overall pregestational diabetes) was ascertained through the KPNC Diabetes Registry. Study methods and description of the KPNC Diabetes Registry (99% sensitivity based on chart review validation) have been published previously.^{15, 16} Briefly, in the Diabetes Registry, clinical recognition of diabetes is based on meeting any of the following criteria: 1) inpatient diagnosis of diabetes (principal diagnosis of ICD-9: 250); 2) two or more outpatient diagnoses of diabetes with ICD-9: 250 (excluding those collected in the emergency room, optometry or ophthalmology departments); 3) outpatient laboratory test result for HbA1c > 6.7; or 4) pharmacy utilization (prescription for insulin or oral antihyperglycemic medications). Women are excluded from the Diabetes Registry if they are identified for the use of insulin sensitizers (thiazolidinediones or metformin), conditions other than diabetes (e.g., lipodystrophy or polycystic ovarian syndrome), or if they were identified for one of the four criteria without a subsequent diabetes related utilization within a 2 year period. Women were excluded from this study if, for a given pregnancy, they had gestational diabetes (ICD-9: 648.8) or met the diagnostic glucose thresholds for gestational diabetes according to the Carpenter and Coustan criteria,¹⁸ as assessed by linking with the KPNC Pregnancy Glucose Tolerance and Gestational Diabetes Registry.¹⁷

Pregestational diabetes types were defined using a combination of ICD-9 codes and insulin use as follows: a) identified as pregestational type 2 diabetes if insulin was never used or used only during pregnancy (n= 3,200), or if insulin was used during pregnancy and in the year prior to conception and only ICD-9 codes for type 2 diabetes (ICD-9 250.x0, 250.x2) were present and no ICD-9 codes for type 1 diabetes (ICD-9 250.x1, 250.x3) were present (n=772); b) identified as pregestational type 1 diabetes if insulin was used during pregnancy and in the year prior to conception and ICD-9 codes for type 1 diabetes were present (n= 1,250). Diabetes type was assigned unknown if neither of the above definitions were met and the pregnancy excluded (n=34). Among the 1,250 pregnancies defined as having pregestational type 1 diabetes, approximately 90% of them had at least two diagnoses of type 1 diabetes on different occasions.

Maternal age was obtained from EHR and self-reported race-ethnicity was obtained from the birth certificate. This study was approved by the human subjects committees of KPNC and the State of California.

Statistical Analyses

The age-adjusted prevalence of pregestational diabetes per 100 deliveries (95% Confidence Interval) was obtained from logistic regression analyses conducted among 655,428 pregnancies delivering ≥ 20 weeks gestation in 1996–2014. Time trends in the age-adjusted prevalence of overall pregestational diabetes, pregestational type 1 and type 2 diabetes (per 100 deliveries) were evaluated among all women and by race-ethnicity, with years grouped 1996–1999, 2000–2002, 2003–2005, 2006–2008, 2009–2011 and 2012–2014. Differences by race-ethnicity were obtained from logistic regression models that included the racial-ethnic groups as dummy variables. The p-values for the parameters calculated for each racial-ethnic group were obtained from maximum likelihood estimation. All analyses were performed using SAS 9.3.

RESULTS

Among 655,428 pregnancies delivered at ≥ 20 weeks gestation between January 1, 1996 and December 31, 2014 at KPNC, 5,256 (0.8%) pregnancies were identified as affected by pregestational diabetes. Of these, 1,250 (23.8%) were classified as type 1 diabetes and 3,972 (75.6%) as type 2 diabetes; for 34 (0.6%) pregnancies, diabetes type was classified as unknown and the pregnancies excluded. Table 1 presents characteristics of the study cohort according to pregestational diabetes status and type. Women with pregestational type 2 diabetes were more likely to be older (i.e. aged 30 years or beyond) than both women without pregestational diabetes and women with pregestational type 1 diabetes. As compared with women without pregestational diabetes, women with pregestational type 1 diabetes were more likely to be non-Hispanic White, while women with pregestational type 2 diabetes were more likely to be African American, Asian or Hispanic.

Table 2 displays the crude and age-adjusted prevalence of overall pregestational diabetes per 100 deliveries. The age-adjusted prevalence of overall pregestational diabetes increased from 1996–1999 to 2009–2011 and then leveled off in 2012–2014 (from 0.58 [95% CI 0.54–0.63] to 1.06 [1.00–1.12] per 100 deliveries; $P_{\text{trend}} < 0.0001$). Increases in the age-adjusted prevalence of overall pregestational diabetes were observed for all racial-ethnic groups (all $P_{\text{trend}} < .0001$); the largest relative increases were observed among Hispanic women (121.8% [84.4, 166.7]), while the smallest relative increases were observed among non-Hispanic White women (49.6% [27.5, 75.4]).

Significant increases in the prevalence of both pregestational type 1 and type 2 diabetes were observed (Tables 3 and 4). The age-adjusted prevalence of type 1 diabetes increased from 1996–1999 to 2009–2011 and then leveled off in 2012–2014 (from 0.14 [0.12–0.16] in 1996–1999 to 0.24 [0.21–0.27] per 100 deliveries in 2012–2014; $P_{\text{trend}} < .0001$) (Table 3). The age-adjusted prevalence of type 2 diabetes increased from 1996–1999 to 2012–2014 (from 0.42 [0.38–0.46] to 0.78 [0.73–0.83] per 100 deliveries; $P_{\text{trend}} < .0001$) (Table 4). Racial and ethnic disparities were observed for trends in the age-adjusted prevalence of pregestational

type 1 and type 2 diabetes (Tables 3 and 4). From 1996–1999 to 2012–2014, non-Hispanic White women had the largest relative increase in the age-adjusted prevalence of pregestational type 1 diabetes (118.4% [70.0, 180.5]; $P_{\text{trend}} < .0001$), and the smallest relative increases in the age-adjusted prevalence of pregestational type 2 diabetes (13.6% [−8.0, 40.1]; $P_{\text{trend}} > .05$). From 1996–1999 to 2012–2014, Hispanic women had the largest relative increases in the age-adjusted prevalence of pregestational type 2 diabetes (125.2% [84.8, 174.4]; $P_{\text{trend}} < .0001$) and a large increase in the age-adjusted prevalence of pregestational type 1 diabetes (88.3% [12.5, 215.3]; $P_{\text{trend}} < .0001$). African American and Asian women had small, statistically non-significant relative changes in the age-adjusted prevalence of pregestational type 1 diabetes from 1996–1999 to 2012–2014 (17.0% [−38.1, 121.4] and −18.4% [−57.2, 55.4], respectively; $P_{\text{trend}} > .05$) and large, statistically significant increases in the age-adjusted prevalence of pregestational type 2 diabetes from 1996–1999 to 2012–2014 (102.0% [38.3, 194.3] and 93.3% [48.9, 150.9], respectively; $P_{\text{trend}} < .0001$).

In 2012–2014, the highest age-adjusted prevalence of pregestational type 1 diabetes was observed in non-Hispanic White women (0.36 per 100 deliveries [0.31, 0.43]), followed by African American women (0.27 per 100 deliveries [0.17, 0.43]). However, the prevalence estimates for non-Hispanic White women were only significantly higher than the prevalence estimates observed for Hispanic (0.16 per 100 deliveries [0.11, 0.22]) and Asian women (0.09 per 100 deliveries [0.06, 0.14]; both p values < 0.0001). In contrast, the highest age-adjusted prevalence of pregestational type 2 diabetes was observed in Hispanic women (1.42 per 100 deliveries [1.26, 1.59]), followed by African American (1.11 per 100 deliveries [0.88, 1.39]) and Asian women (0.83 per 100 deliveries [0.71, 0.95]), and each of these prevalence estimates were statistically significantly higher than the prevalence estimate observed for non-Hispanic White women (0.39 per 100 deliveries [0.33, 0.45]); all p values < 0.0001).

COMMENTS

In a large, diverse cohort of pregnant women, we observed an alarming 81.3% increase in the prevalence of overall pregestational diabetes between 1996–1999 and 2012–2014. Prevalence increases were observed for both type 1 and type 2 diabetes, and significant racial and ethnic disparities in the relative prevalence increases were observed for type 1 and type 2 diabetes.

The increase in the prevalence of pregestational diabetes may be due to increases in the proportion of diabetic women able to become and remain pregnant through 20 weeks of gestation, and is likely related to improvements in preconception and prenatal care for women with diabetes. The observed increase in the prevalence of pregestational diabetes may also be due to increases in the incidence of diabetes among reproductive aged women. Although increases in the incidence of type 1 diabetes have also been reported,^{19, 20} the causes are largely unknown. Increases in the incidence of type 2 diabetes are mostly likely due to increases in the prevalence of overweight and obesity among women of reproductive age in the U.S during the study period.^{21, 22}

We observed significant racial-ethnic disparities in the increases in the prevalence of pregestational diabetes overall and by sub-type. Non-Hispanic White women had the largest relative increase in the prevalence of pregestational type 1 diabetes and the smallest relative increase in pregestational type 2 diabetes. Women from racial-ethnic minority groups (Hispanic, African American and Asian women) experienced dramatic increases in the prevalence of pregestational type 2 diabetes, specifically, higher relative increases than that observed among non-Hispanic White women. The disproportionate increase in pregestational type 2 diabetes among racial-ethnic minority groups is likely due, in part, to increases in the prevalence of overweight and obesity among African American and Hispanic women in the U.S during the study period; however, national data lack information on trends in overweight and obesity among Asian women.^{21, 22}

Our findings are in agreement with previous studies reporting trends in the prevalence of pregestational diabetes in the U.S. and Canada. The most recent study, which used hospital discharge data from 19 U.S. states, reported that age-standardized prevalence of pregestational diabetes increased from 0.65% per 100 deliveries in 2000 to 0.89% per 100 deliveries in 2010.⁴ A study at Kaiser Permanente Southern California found that the age and race-ethnicity adjusted prevalence of pregestational diabetes more than doubled between 1999 and 2005 (from 0.81 to 1.82 per 100 deliveries).² A large, population-based in Ontario, Canada, similarly revealed that the age-adjusted prevalence of pregestational diabetes doubled between 1996 and 2010.²³ The only previous study examining trends in the prevalence of pregestational type 1 and type 2 diabetes was conducted for 1994 to 2004, used hospital discharge diagnoses to define diabetes type and did not have data on race-ethnicity;³ nevertheless, the reported increases in type 1 and type 2 diabetes were similar to those observed in our population up to 2004: the crude prevalence of type 1 increased from 0.24% to 0.33% per 100 deliveries, while the prevalence of type 2 diabetes increased from 0.24% to 0.84% per 100 deliveries.³

The increased prevalence of pregestational diabetes is consistent with reports of substantial increases in the prevalence of diabetes in the U.S. population in general over the past two decades²⁴ and is of great concern due to the increased risk of maternal and neonatal complications associated with pregestational diabetes. In addition, given the growing body of evidence suggesting that *in utero* exposure to diabetes is associated with increased risk of obesity and diabetes in the offspring,^{25, 26} increases in pregestational diabetes suggest a snowballing of the inter-generational transfer of these chronic conditions.

The main strength of the current study is the use of the KPNC Diabetes Registry^{15, 16} to assess diabetes status prior to conception, in addition to utilizing data on insulin use (in the year prior to conception and during pregnancy) and ICD-9 codes to classify women as having type 1 or type 2 diabetes. Although we were unable to validate our classification scheme against etiologic criteria (i.e., presence of antibodies for type 1 and the presence of insulin resistance for type 2), previous investigations of trends in pregestational diabetes were either unable to assess diabetes type^{2, 4} or relied on hospital discharge diagnosis at delivery for the designation of diabetes type.³ In addition, our results are consistent with race-ethnic specific trends in prevalence of type 1 diabetes reported among youth in the U.S. up to 2009 in the SEARCH study,²⁷ where type 1 diabetes was defined by physician

diagnosis and validated by etiologic criteria, such as presence of diabetes antibody. The use of the KPNC Pregnancy Glucose Tolerance and Gestational Diabetes Registry¹⁷ to identify and exclude women with gestational diabetes, as determined by objective glucose measurements, is another strength.

BMI data were unavailable and thus we were not able to control for trends of increases in the prevalence maternal obesity. Trends in maternal BMI may have explained, at least in part, the observed increases in the prevalence of type 2 diabetes, as well as the observed racial and ethnic disparities. The racial and ethnic disparities observed in this study may not be generalizable to analyses utilizing more granular categories of race-ethnicity. In addition, differential rates of early fetal loss between type 1 and type 2 diabetes could have introduced bias to our study, though available evidence suggests that such differential rates of fetal loss are unlikely.²⁸

In summary, the prevalence of overall pregestational diabetes and pregestational type 1 and type 2 diabetes increased from 1996–1999 to 2012–2014. Significant racial-ethnic disparities were observed for the increases in pregestational type 1 and type 2 diabetes. Given the increased prevalence of pregestational diabetes in pregnant women and projections for sustained or further increases in subsequent generations, prevention strategies and health system based interventions of preconception care targeting young women, especially those from minority groups, are needed to optimize the health of mothers and their infants and to reduce the health care cost of diabetes.

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Table 1

Characteristics of the study cohort by pregestational diabetes status: Kaiser Permanente Northern California 1996–2014.

	Pregnancies without recognized pregestational diabetes (N=650,206)	Pregnancies with pregestational type 1 diabetes (N= 1,250)	Pregnancies with pregestational type 2 diabetes (N= 3,972)
	n (%)	n (%)	n (%)
Age, years			
<20 years	37,138 (5.7%)	51 (4.1%)	39 (1.0%)
20–29 years	282,628 (43.5%)	518 (41.4%)	900 (22.7%)
30–39 years	300,207 (46.2%)	620 (49.6%)	2,550 (64.2%)
40+ years	26,116 (4%)	58 (4.6%)	469 (11.8%)
Missing	4,117 (0.6%)	3 (0.2%)	14 (0.3%)
Race-Ethnicity			
Non-Hispanic White	262,362 (40.4%)	716 (57.3%)	973 (24.5%)
African American	46,190 (7.1%)	119 (9.5%)	413 (10.4%)
Asian	121,906 (18.7%)	109 (8.7%)	915 (23.0%)
Hispanic	159,007 (24.5%)	241 (19.3%)	1,377 (34.7%)
Other	47,223 (7.3%)	53 (4.2%)	248 (6.2%)
Missing	13,518 (2.1%)	12 (1.0%)	46 (1.2%)

Time trends in the crude and age-adjusted prevalence of overall pregestational diabetes (95% Confidence Interval) per 100 deliveries by race/ethnicity: Kaiser Permanente Northern California 1996–2014.

Table 2

	1996–1999 (n= 124,825)	2000–2002 (n= 102,060)	2003–2005 (n= 103,701)	2006–2008 (n= 109,200)	2009–2011 (n= 104,901)	2012–2014 (n=110,775)	% Change ^a	P for trend
All women								
Crude	0.50	0.57	0.76	0.91	1.03	1.04	108	
Age-adjusted	0.58	0.65	0.82	0.98	1.08	1.06	82.5	<.0001
Non-Hispanic White								
Crude	0.49	0.52	0.64	0.72	0.75	0.78	59.2	
Age-adjusted	0.54	0.57	0.68	0.77	0.79	0.80	49.6	<.0001
African American								
Crude	0.64	1.02	1.42	1.30	1.32	1.25	95.3	
Age-adjusted	0.81	1.24	1.68	1.59	1.54	1.41	75.8	<.0001
Asian								
Crude	0.53	0.44	0.60	0.92	1.09	1.09	106	
Age-adjusted	0.55	0.45	0.59	0.87	0.99	0.96	73.8	<.0001
Hispanic								
Crude	0.57	0.65	1.05	1.08	1.29	1.49	161	
Age-adjusted	0.74	0.81	1.23	1.26	1.44	1.63	121.8	<.0001

^aIndicates rate change from 1996–1999 to 2012–2014 prevalence estimates

Time trends in the crude and age-adjusted prevalence of pregestational type 1 diabetes (95% Confidence Interval) per 100 deliveries by race/ethnicity: Kaiser Permanente Northern California 1996–2014.

Table 3

	1996–1999 (n= 124,825)	2000–2002 (n= 102,060)	2003–2005 (n= 103,701)	2006–2008 (n= 109,200)	2009–2011 (n= 104,901)	2012–2014 (n=110,775)	% Change ^a	P for trend
All								
Crude	0.13	0.13	0.18	0.20	0.28	0.23	76.9	
Age-adjusted	0.14	0.13	0.19	0.20	0.29	0.24	73.2	<.0001
Non-Hispanic White								
Crude	0.17	0.18	0.25	0.29	0.39	0.38	124	
Age-adjusted	0.17	0.17	0.24	0.28	0.37	0.36	118.4	<.0001
African American								
Crude	0.20	0.23	0.34	0.21	0.33	0.24	20.0	
Age-adjusted	0.23	0.26	0.38	0.24	0.37	0.27	17.0	0.43
Asian								
Crude	0.10	0.03	0.10	0.09	0.12	0.08	-20.0	
Age-adjusted	0.11	0.04	0.11	0.10	0.13	0.09	-18.4	0.57
Hispanic								
Crude	0.08	0.09	0.16	0.16	0.26	0.16	100	
Age-adjusted	0.08	0.09	0.17	0.16	0.26	0.16	88.3	<.0001

^aIndicates rate change from 1996–1999 to 2012–2014 prevalence estimates

Time trends in the crude and age-adjusted prevalence of pregestational type 2 diabetes (95% Confidence Interval) per 100 deliveries by race/ethnicity: Kaiser Permanente Northern California 1996–2014.

Table 4

	1996–1999 (n= 124,825)	2000–2002 (n= 102,060)	2003–2005 (n= 103,701)	2006–2008 (n= 109,200)	2009–2011 (n= 104,901)	2012–2014 (n=110,775)	% Change ^a	P for trend
All								
Crude	0.37	0.44	0.57	0.71	0.75	0.81	119	
Age-adjusted	0.42	0.49	0.60	0.73	0.75	0.78	85.2	<.0001
Non-Hispanic White								
Crude	0.31	0.34	0.39	0.42	0.37	0.40	29.0	
Age-adjusted	0.34	0.36	0.40	0.43	0.36	0.39	13.6	0.24
African American								
Crude	0.44	0.79	1.09	1.09	0.99	1.01	129	
Age-adjusted	0.55	0.95	1.27	1.32	1.13	1.11	102.0	0.0004
Asian								
Crude	0.44	0.41	0.50	0.83	0.97	1.01	130	
Age-adjusted	0.43	0.40	0.46	0.74	0.82	0.83	93.3	<.0001
Hispanic								
Crude	0.49	0.56	0.89	0.92	1.03	1.34	173	
Age-adjusted	0.63	0.69	1.01	1.04	1.12	1.42	125.2	<.0001

^aIndicates rate change from 1996–1999 to 2012–2014 prevalence estimates