Published in final edited form as:

Obstet Gynecol. 2008 October ; 112(4): 875–883. doi:10.1097/AOG.0b013e31818638b5.

Cardiovascular Disease Risk Profiles in Women with Histories of Gestational Diabetes but Without Current Diabetes

Catherine Kim, MD MPH

Departments of Medicine and Obstetrics & Gynecology, University of Michigan, Ann Arbor, MI

Yiling J. Cheng, MD PhD

Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, GA

Gloria L. Beckles, MD MSc

Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, GA

Abstract

Objective—To compare the cardiovascular disease risk factor profiles of parous women with a history of gestational diabetes who had not developed diabetes, parous women with diagnosed diabetes, and parous women with neither condition.

Methods—We conducted cross-sectional analyses of 4,631 parous women who were not currently pregnant in the Third National Health and Nutrition Examination Survey (1988–1994). Women were classified by self-report as having a history of gestational diabetes who were not currently diabetic ($n=85$), diagnosed diabetics ($n=218$), or as having neither condition ($n=4,328$). We compared these groups with respect to cholesterol subtypes, blood pressure, uric acid, microalbuminuria, insulin, and glucose, and clustering of risk factors, before and after adjustment for demographic and behavioral factors and central obesity.

Results—In unadjusted comparisons, women who had a history of gestational diabetes who were not currently diabetics had a more favorable or similar risk factor profile compared to unaffected women, with two exceptions: greater levels of mean fasting glucose (94.0 mg/dl vs. 106.8 mg/dl, $p<0.001$) and mean fasting insulin (10.2 IU/l vs. 14.0 IU/l, $p<0.001$). These patterns were attenuated after adjustment for demographic factors and waist circumference, but remained significant for fasting glucose and the ratio of urine microalbumin/creatinine. Parous women with diagnosed diabetes had significantly worse cardiovascular disease risk profiles than unaffected women before and after adjustment.

Conclusions—Women who had a history of gestational diabetes who were not currently diabetics have a similar cardiovascular disease risk profile to unaffected women, with the exception of insulin and glucose levels.

Introduction

Gestational diabetes is defined as glucose intolerance first identified during pregnancy (1). While this glucose intolerance resolves with delivery in about 90% of cases (2), women with

Address for correspondence: Catherine Kim, MD MPH 300 NIB, Room 7C13 Ann Arbor, MI 48109 Telephone: (734) 647-9688 Fax: (734) 936-8944 e-mail: cathkim@umich.edu.

Financial Disclosure: The authors have no potential conflicts of interest to disclose.

Presented in part at the 68th Scientific Sessions of the American Diabetes Association, San Francisco, CA, June 6–10, 2008.

Precis Women with a history of gestational diabetes who are not currently diabetic have similar cardiovascular risk profiles to unaffected women.

histories of gestational diabetes are at increased risk of developing diabetes, the metabolic syndrome, and cardiovascular disease (3-8). A previous study suggests that despite normal glucose levels, women with histories of gestational diabetes have less favorable cardiovascular risk factors compared to unaffected women (8).

The degree to which women with histories of gestational diabetes are at risk for cardiovascular disease, beyond their predisposition to future diabetes, is unclear. Women with histories of gestational diabetes may be at increased risk of cardiovascular disease primarily through their development of diabetes, or alternatively may be at increased risk of cardiovascular disease even if they have not developed diabetes. Using the National Health and Nutrition Examination Survey III (NHANES III), a population-based cross-sectional study, we examined levels of cardiovascular risk factors and the number of risk factors along with Metabolic syndrome components. We compared unaffected parous women, women with histories of gestational diabetes who had not been identified with diagnosed diabetes, and women with diagnosed diabetes. We hypothesized that risk factor levels and clustering of risk factors would be progressively elevated among unaffected women vs. women with histories of gestational diabetes vs. women with diagnosed diabetes. We also hypothesized that these associations would be attenuated after adjustment for risk factors, particularly for waist circumference.

Materials and Methods

Study Population

The study population was a sample from the NHANES III, which was conducted using a multistage sampling design representative of the non-institutionalized civilian population in the U.S. between 1988 and 1994. A detailed description of the objectives and data collection procedures of the NHANES III has been reported previously (9). Briefly, each NHANES wave consists of a detailed standardized medical examination in a mobile examination unit and an interview to obtain information on sociodemographic characteristics and cardiovascular risk factors. Participants were selected at random for fasting glucose testing. The selection process was as follows: each household was randomly assigned to either a morning or an afternoon/evening examination session. Plasma glucose values were not obtained for people who did not participate in the examination (n = 811), were examined at home where fasting was not required (n = 209), were examined in the afternoon/evening (n = 311), had medical and safety reasons for exclusion (n = 10), became faint or ill (n = 2), refused the venipuncture (n = 28), had unsuccessful venipuncture (n = 27), fasted for <9 h (n = 369) or < 24 h (n = 8), or had an unknown fasting time (n = 89), and for other reasons (n = 137). Plasma glucose values were obtained after an overnight fast of 9 to <24 h for 6,587 people (77%). There were no statistically significant differences in a variety of sociodemographic and clinical variables between subjects assigned to the morning session versus subjects assigned to the afternoon/evening session. In addition, for those in the morning session, there were no significant differences between subjects for whom plasma glucose values were obtained versus those for whom plasma glucose values were not obtained. Thus, data from the subsamples are considered to represent the entire NHANES III sample (10). For the purposes of this report, we excluded women who were nulliparous, pregnant at the time of data collection, or had missing data regarding pregnancy status or previous diabetes or histories of gestational diabetes diagnoses, for a total sample of 4631 women. This study was declared IRB exempt by the University of Michigan IRB.

Exposure Assessment

Parous women were stratified based on their health status at the time of the NHANES interview and categorized hierarchically based on their risk strata as having diabetes, histories of gestational diabetes, or neither condition. Women were asked, 1) Have you every been told by

a doctor that you have diabetes or sugar diabetes? 2) Were you pregnant when you were told you had diabetes? 3) Other than pregnancy, has a doctor ever told you that you have diabetes or sugar diabetes? Based on these questions, women were classified as having diagnosed diabetes if they reported a diagnosis of diabetes, either type 1 diabetes or type 2 diabetes, outside of pregnancy (n=4328)(11). Women were classified as having histories of gestational diabetes without current diabetes if they reported having a diagnosis of diabetes made during pregnancy and no diagnosed diabetes at interview (n=85). Women were classified as unaffected if they did not have histories of gestational diabetes or diagnosed diabetes (n=218); As we were focused on the risk factor profile of women with histories of gestational diabetes who had not yet developed diabetes, women who had diabetes and histories of gestational diabetes (n=29) were classified as having diagnosed diabetes. In the NHANES III, it is not possible to combine participants with diagnosed and undiagnosed diabetes for risk analysis, since the denominator for the estimate of undiagnosed diabetes is different from the one for the estimate of diagnosed diabetes; undiagnosed diabetes was assessed in a subsample of nondiabetic persons who were randomly assigned to a morning fasting examination, whereas diagnosed diabetes was assessed for the entire sample. Therefore, for the purposes of this report, fasting glucose levels were not used to identify women with diagnosed diabetes.

Information on age, sex, race/ethnicity, family history of diabetes, income, smoking, and alcohol intake were collected by interview (9). Women were classified as having a family history of diabetes if a first-degree relative (biological parents or siblings) had diabetes. The poverty index was calculated using self-reported family income and the poverty threshold value produced annually by the U.S. Census Bureau (12). Measurements of height, weight, and waist circumference were performed in a standardized manner, and body mass index (BMI) was calculated as weight in kilograms divided height in meters squared. Leg length, a measure of early life socioeconomic deprivation, was calculated by subtracting sitting height from standing height (13,14). A history of cardiovascular events was determined if women answered “yes” to any of the following questions: 1) Has a doctor ever told you had a heart attack? 2) Has a doctor ever told you had a stroke? 3) Has a doctor ever told you that you had congestive heart failure?

Main Outcome Measures

We defined risk factors for cardiovascular disease using the Adult Treatment Panel III guidelines (15). Cardiovascular risk factors included self-report of the following risk factors: age over 55 years, family history of cardiovascular disease, current cigarette smoking, presence of diabetes, hypertension, or dyslipidemia. Family history of cardiovascular disease was defined as a first degree male relative with cardiovascular disease younger than 55 years of age or a first degree female relative with cardiovascular disease at less than 65 years of age. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg upon examination, or participant report of physician-diagnosed hypertension on at least 2 occasions with current use of anti-hypertensive medication. Dyslipidemia was defined as a total cholesterol ≥ 240 mg/dl or participant report of physician-diagnosed dyslipidemia that was currently treated with lifestyle modification or medication.

Metabolic syndrome was defined as the presence of ≥ 3 of any of the following components: waist circumference ≥ 35 inches; systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg; fasting blood glucose ≥ 110 mg/dl (≥ 6.1 mmol/l); serum high-density lipoprotein cholesterol level (HDL) ≤ 50 mg/dl (≤ 1.29 mmol/l); and total triglyceride level ≥ 150 mg/dl (≥ 1.69 mmol/l) (16). If participants used hypertensive medication or statin medication, they were classified as having elevated blood pressure or dyslipidemia respectively. Newer criteria for Metabolic syndrome use the fasting blood glucose cut-off of 100 mg/dl, but we used the older definition as this was the one in use when the data were

collected. Levels of low-density lipoprotein cholesterol (LDL), triglycerides, insulin, and glucose were estimated using the morning fasting sample of participants; insulin and glucose were not measured on persons with diagnosed diabetes who were on insulin therapy. Albuminuria is expressed as milligrams per gram of creatinine: normal (<30 mg/g Cr), microalbuminuria (≥ 30 to 299 mg/g Cr), and macroalbuminuria (≥ 300 mg/g Cr) (17).

Statistical analysis

All analyses accounted for the complex, multistage, stratified, cluster-sampling design of NHANES III by using sample weights, strata, and primary sampling units provided by the survey designer as part of the public data. First, we compared unaffected women, women with histories of gestational diabetes, and women with diagnosed diabetes across exposure and outcome variables. For continuous variables, we conducted tests of trend using the Fisher-Yates test, and for categorical variables, we conducted chi-square tests. In multivariable models, we calculated predicted marginal probabilities and 95% confidence intervals for levels of individual cardiovascular risk factors and metabolic syndrome components (18).

Multivariable models were constructed in several stages. The first set of models (Model 1) adjusted for age, race/ethnicity, family history of diabetes, cigarette smoking, and alcohol intake. Next, we added waist circumference, a measure of central obesity (Model 2). The third set of models also adjusted for self-reported cardiovascular disease (Model 3). The next model also adjusted for leg length (Model 4). The last model also adjusted for the poverty-index ratio as a measure of current, rather than early-life, socioeconomic deprivation (Model 5). Due to the fact that both leg-length and education are measures of early-life deprivation (13,14), we used leg-length rather than education in the models.

We also constructed multivariable models for the presence of metabolic syndrome (yes/no), defined as the presence ≥ 3 metabolic syndrome components, as well as adjusted models for the presence of ≥ 3 cardiovascular risk factors. Adjusted predicted marginal probabilities were estimated from each model and used to calculate adjusted prevalence ratios for the histories of gestational diabetes and diagnosed diabetes groups (referent group, unaffected women). Due to the small number of cardiovascular events, we did not examine actual cardiovascular events as an outcome. The models examining metabolic syndrome did not additionally adjust for waist circumference, as these were already included in the definition of metabolic syndrome. Statistical analyses were conducted using SUDAAN 9.0 (Research Triangle Institute, North Carolina) software.

Results

The characteristics of women in our sample are illustrated in the first section of Table 1. Women with diagnosed diabetes were significantly older than women with histories of gestational diabetes or unaffected women and were more likely to report African-American or Non-Hispanic Black race/ethnicity, family history of diabetes, the least favorable poverty to income ratios, the fewest number of alcoholic drinks per day, and the greatest waist circumferences. Unaffected women tended to have the longest leg length and women with histories of gestational diabetes more often tended to be current smokers, but these associations were not significant.

In unadjusted comparisons, women with diagnosed diabetes had worsened levels of cardiovascular and metabolic syndrome factors than unaffected women (Table 1). In comparison, differences between women with histories of gestational diabetes and unaffected women were less marked. Women with histories of gestational diabetes actually had more favorable cholesterol subtypes and blood pressure levels than unaffected women. The exceptions were fasting insulin and glucose levels. Fasting insulin and glucose did increase

across categories of glucose intolerance (Table 1). When we examined the number of metabolic syndrome components or cardiovascular risk factors, which dichotomized risk factor levels, the number of components was greatest in women with diagnosed diabetes, followed by women with histories of gestational diabetes. Self-reported cardiovascular was uncommon, reported in 6.7% (n=18) of women with diagnosed diabetes, 0.7% (n=2) of women with histories of gestational diabetes, and 1.6% (n=91) of unaffected women (p=0.048).

Adjusted Models

When we adjusted for patient covariates, the largest differences were again seen between women with diagnosed diabetes and other groups (Table 2). After adjustment for age, race/ethnicity, family history of diabetes, cigarette smoking, and alcohol intake (Table 2, Model 1), women with diagnosed diabetes had similar risk factor patterns compared to unadjusted analyses. Women with diagnosed diabetes had poorer LDL, HDL, total cholesterol, systolic blood pressure, insulin, glucose, and microalbumin levels than unaffected women. The exception to this pattern was that uric acid levels, triglyceride levels, and diastolic blood pressure levels no longer differed significantly. Women with diagnosed diabetes were also more likely to have metabolic syndrome and to have ≥ 3 cardiovascular risk factors than unaffected women. Women with diagnosed diabetes also had poorer HDL and total cholesterol, fasting glucose, and microalbuminuria than women with histories of gestational diabetes.

After adjustment (Table 2, Model 1), women with histories of gestational diabetes still tended to have more favorable risk factor levels compared to unaffected women, although these comparisons were not significant. Women with histories of gestational diabetes had a similar chance of having metabolic syndrome and of having ≥ 3 cardiovascular risk factors as unaffected women.

After additional adjustment for waist circumference (Model 2), women with diagnosed diabetes no longer differed in their HDL cholesterol levels or systolic blood pressure levels from unaffected women, but the greater presence of microalbuminuria and elevated insulin, glucose, and total cholesterol persisted. Women with diabetes were still more likely than unaffected women to have ≥ 3 cardiovascular risk factors compared to unaffected women. After additional adjustment for waist circumference (Model 2), women with diagnosed diabetes still had worsened microalbuminuria, insulin, glucose, and total cholesterol compared to women with histories of gestational diabetes. After adjustment for waist circumference, women with histories of gestational diabetes were still more likely to have ≥ 3 cardiovascular risk factors compared to unaffected women. The addition of waist circumference to demographic risk factors (Model 2) explained a significantly greater proportion of variance than demographic factors alone (Model 1). When waist circumference was not included as an adjuster, as was the case when metabolic syndrome was the outcome, the R^2 for multivariable models was much lower than the R^2 for the cardiovascular models where the outcome was also dichotomous.

Further adjustment for cardiovascular, leg length, and poverty-index-ratio did not change this pattern for individual cardiovascular risk factors or for the metabolic syndrome and number of cardiovascular risk factors (results not shown). Of note, the additional proportion of variance or the increase in R^2 in Models 3, 4, and 5 tended to be slight compared to Models 1 and 2. In other words, models adjusting for demographic factors, behavioral factors, and waist circumference explained similar variance to models that also adjusted for cardiovascular, leg-length, and poverty-index-ratio. This may be because the number of cardiovascular events was low and only small differences in leg-length were observed, and/or the effects of these factors were mediated through others.

Sensitivity Analyses

In sensitivity analyses, we substituted BMI for waist circumference to determine if this increased the explained variance of the model or otherwise changed point estimates. We found that these BMI models had slightly lower R^2 than models with waist circumference and did not have point estimates that differed significantly from models using waist circumference (results not shown). Therefore, we report results with waist circumference. Relatively few women had microalbuminuria levels that were >30 ug/G, so in multivariable models, the urine microalbuminuria/creatinine was dichotomized as <30 ug/G vs. > 30 ug/G and the results expressed in predicted marginal probabilities. We examined whether using the newer cut-off of FPG=100 mg/dl impacted the metabolic syndrome definition; proportions were not significantly different (results not shown). Finally, among women classified as histories of gestational diabetes, 8 (9.4%) had fasting glucose levels > 126 mg/dl and among women classified as unaffected by either histories of gestational diabetes or diagnosed diabetes, 50 (1.2%) had fasting glucose levels > 126 mg/dl. In a sensitivity analysis, we examined only women who had a fasting glucose as well as fasting glucose levels < 126 mg/dl ($n=1900$), but this did not alter our pattern of effects, so the larger sample is included in this report.

Discussion

This cross-sectional study of the female population of the U.S. suggests that women with histories of gestational diabetes who have not developed diagnosed diabetes had similar levels of each metabolic syndrome factor and each cardiovascular risk factor compared to unaffected women, with the exception of insulin and glucose levels. When factors were dichotomized, women with histories of gestational diabetes only had only a slightly greater number of metabolic syndrome components and cardiovascular risk factors than unaffected women. In contrast, women with diagnosed diabetes had a significantly worsened profile than other women.

In a cross-sectional analysis of GENNID, Carr and colleagues found that women with histories of gestational diabetes were more likely to have metabolic syndrome and to experience cardiovascular events than women without histories of gestational diabetes, and moreover, that these cardiovascular events occurred at a younger age (8). In their study, the definitions of histories of gestational diabetes and diagnosed diabetes were not mutually exclusive, so that $>90\%$ of women with histories of gestational diabetes had developed diabetes and 63% of the women without histories of gestational diabetes had developed diabetes. The high prevalence of diabetes was presumably due to the study requirement that at least 2 first degree relatives be affected by diabetes. Other studies have documented the presence of metabolic syndrome among women with histories of gestational diabetes as well (5,19,20). Our results may have differed from these studies for several reasons. Carr and colleagues examined a population at extremely high risk for diabetes, whereas we examined a population-based sample. Similarly, for other hospital-based analyses, it is possible that the women with histories of gestational diabetes who return for follow-up represent a higher-risk cohort, perhaps having greater glucose dysregulation during pregnancy. Second, we surmise that women with histories of gestational diabetes at highest risk for diabetes (and other risk factors) may have already developed the condition prior to their NHANES interview and thus only women at lower risk for diabetes (and other risk factors) remain in the histories of gestational diabetes sample. Had we been able to examine women closer to delivery, before anyone in the cohort developed diabetes, we might have detected greater differences in cardiovascular risk factors or metabolic syndrome components (4).

The women with histories of gestational diabetes in our study may have fairly benign risk factor profiles for reasons other than their lack of development of diabetes. It is possible that inadequate time has elapsed to allow progression of their profiles. However, after we adjusted

for age, the relationship was not changed. In addition, women with histories of gestational diabetes had similar leg length to women with diagnosed diabetes, suggesting that they had experienced similar deprivation in early life. Alternatively, women with histories of gestational diabetes who do not develop diagnosed diabetes may be healthier than women with histories of gestational diabetes who do develop diagnosed diabetes, or women with histories of gestational diabetes may have had their risks of early-life deprivation modified by improved circumstances in later life (21). Along these lines, women with histories of gestational diabetes may have adopted lifestyle changes that prevent them from developing diabetes and also improved their cardiovascular risk profile. However, in other population-based surveys, the physical activity level and dietary intake of women with histories of gestational diabetes were poor (22).

The addition of waist circumference to the multivariable models notably increased the proportion of variance in cardiovascular risk factor levels explained by the models, beyond the variance explained by demographic factors and behavioral factors such as alcohol intake. Greater waist circumference accounted for differences in HDL cholesterol and blood pressure levels between women with diabetes vs. unaffected women and women with diabetes vs. women with histories of gestational diabetes, although it did not account for differences in glucose and insulin. Waist circumference and waist-hip-ratio are commonly used measures of central obesity (23), and the importance of central obesity as an independent predictor of cardiovascular risk as well as mortality has been recognized in prospective cohort studies in women (24,25). Our findings about the poor cardiovascular risk factor profiles of women with diabetes are similar to those of previous studies, particularly in NHANES (26,27).

The study has several limitations. NHANES is cross-sectional, and observations regarding levels of metabolic syndrome components or cardiovascular risk factors across worsening glucose intolerance states do not necessarily reflect disease progression in individuals. As mentioned earlier, we deliberately selected healthier populations by examining women who had not developed diabetes, so our results do not apply to the women with histories of gestational diabetes who develop diabetes. We included about 90 women with histories of gestational diabetes, comparable to others' reports, and while NHANES can distinguish between women with histories of gestational diabetes and women with histories of gestational diabetes and diagnosed diabetes, the numbers of women in these subgroups were too few to allow comparisons.

In conclusion, women with histories of gestational diabetes may have elevated cardiovascular risk, but this risk may be most evident through their risk for diagnosed diabetes. Although we expected to see greater metabolic dysfunction in women with histories of gestational diabetes, this may represent a greater opportunity for prevention for of future glucose intolerance and associated metabolic dysfunction. Postpartum screening after delivery for glucose intolerance and diabetes prevention interventions may also be the most effective measures for lowering of cardiovascular risk.

Acknowledgements

Supported by K23DK071552 from the National Institute of Health of Diabetes and Digestive and Kidney Diseases (NIDDK).

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the funding agency.

References

1. Metzger B, Buchanan T, Coustan D, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care* 2007;30:S251–S260. [PubMed: 17596481]
2. Kjos S, Peters R, Xiang A, Henry O, Montoro M, Buchanan T. Predicting future diabetes in Latino women with gestational diabetes. *Diabetes* 1995;44:586–91. [PubMed: 7729620]
3. Kim C, Newton K, Knopp R. Gestational diabetes and incidence of type 2 diabetes mellitus: a systematic review. *Diabetes Care* 2002;25:1862–8. [PubMed: 12351492]
4. Pallardo F, Herranz L, Garcia-ingelmo T, et al. Early postpartum metabolic assessment in women with prior gestational diabetes. *Diabetes Care* 1999;22:1053–8. [PubMed: 10388966]
5. Pallardo L, Herranz L, Martin-Vaquero P, Garcia-Ingelmo T, Grande C, Janez M. Impaired fasting glucose and impaired glucose tolerance in women with prior gestational diabetes are associated with a different cardiovascular profile. *Diabetes Care* 2003;26:2318–2322. [PubMed: 12882855]
6. Bo S, Monge L, Macchetta C, et al. Prior gestational hyperglycemia: a long-term predictor of the metabolic syndrome. *J Endocrinol Invest* 2004;27:629–35. [PubMed: 15505985]
7. Verma A, Boney C, Tucker R, Vohr B. Insulin resistance syndrome in women with prior history of gestational diabetes mellitus. *J Clin Endocrinol Metab* 2002;87:3227–3235. [PubMed: 12107230]
8. Carr D, Utzschneider K, Hull R, et al. Gestational diabetes mellitus increases the risk of cardiovascular disease in women with a family history of type 2 diabetes. *Diabetes Care* 2006;29:2078–2083. [PubMed: 16936156]
9. National Center for Health Statistics. NHANES III reference manuals and reports. Centers for Disease Control and Prevention; Hyatsville, MD: 1996.
10. Harris M, Flegal K, Cowie C. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults: the Third National Health and Nutrition Examination Survey. *Diabetes Care* 1998;21:518. [PubMed: 9571335]
11. American Diabetes Association. Postpartum screening for gestational diabetes mellitus. In: Kjos, S.; Ratner, R., editors. *Fifth International Workshop on Gestational Diabetes*; Chicago, Illinois. 2005.
12. Wu T, Dorn J, Donahue R, Sempes C, Trevisan M. Associations of serum C-reactive protein with fasting insulin, glucose, and glycosylated hemoglobin. *Am J Epidemiol* 2002;155:65–71. [PubMed: 11772786]
13. Asao K, Kao W, Baptiste-Roberts K, Bandeen-Roche K, Erlinger T, Brancati F. Short stature and the risk of adiposity, insulin resistance, and type 2 diabetes in middle age: the Third National Health and Nutrition Examination Survey (NHANES III), 1988-1994. *Diabetes Care* 2006;29:1632–7. [PubMed: 16801590]
14. Moses R, Mackay M. Gestational diabetes: is there a relationship between leg length and glucose tolerance? *Diabetes Care* 2004;27:1033–5. [PubMed: 15111516]
15. National Heart, Lung, and Blood Institute; Bethesda, MD: 2001. Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): 10-year risk calculator.
16. Grundy S, Brewer H Jr, Cleeman J, et al. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation* 2004;109:433–438. [PubMed: 14744958]
17. American Diabetes Association. Nephropathy in Diabetes. *Diabetes Care* 2004;27:S79–S83. [PubMed: 14693934]
18. Graubard B, Koren E. Predictive margins with survey data. *Biometrics* 1999;55:652–99. [PubMed: 11318229]
19. Noussitou P, Monbaron D, Vial Y, Gaillard R, Ruiz J. Gestational diabetes mellitus and the risk of metabolic syndrome: a population-based study in Lausanne, Switzerland. *Diabetes Med* 2005;31:361–9.
20. Ko G, Chan J, Tsang L, Li C, Cockram C. Glucose tolerance and other cardiovascular risk factors in Chinese women with a history of gestational diabetes mellitus. *Aust NZ J Obstet Gynaec* 1999;39:478–483.

21. Brunner E, Shipley M, Blane D, Smith G, Marmot M. When does cardiovascular risk start? Past and present socioeconomic circumstances and risk factors in adulthood. *J Epidemiol Community Health* 1999;53:757–64. [PubMed: 10656084]
22. Kieffer E, Sinco B, Kim C. Health behaviors in women with a history of gestational diabetes mellitus in the Behavioral Risk Factor Surveillance System. *Diabetes Care* 2006;29:1788–93. [PubMed: 16873781]
23. Snijder M, van Dam R, Visser M, Seidell J. What aspects of body fat are particularly hazardous and how do we measure them? *Int J Epidemiol* 2006;35:83–92. [PubMed: 16339600]
24. Zhang C, Rexrode K, van Dam R, Li T, Hu F. Abdominal obesity and the risk of all-cause, cardiovascular, and cancer mortality: sixteen years of follow-up in U.S. women. *Circulation* 2008;117:1658–67. [PubMed: 18362231]
25. Matthews K, Sowers M, Derby C, et al. Ethnic differences in cardiovascular risk factor burden among middle-aged women: Study of Women's Health Across the Nation (SWAN). *Am Heart J* 2005;149:1066–73. [PubMed: 15976790]
26. Saaddine J, Cadwell B, Gregg E, et al. Improvements in diabetes processes of care and intermediate outcomes: United States, 1988-2002. *Ann Intern Med* 2006;144:465–74. [PubMed: 16585660]
27. Saaddine J, Engelgau M, Beckles G, Gregg E, Thompson T, Narayan K. A diabetes report card for the United States: quality of care in the 1990s. *Ann Intern Med* 2002;136:565–74. [PubMed: 11955024]

Table 1

Unadjusted characteristics of unaffected parous women, women with histories of gestational diabetes, and women with diagnosed diabetes. Means (standard errors) or percentages (standard errors) are shown.

Characteristic	Unaffected women n=4328	Women with histories of gestational diabetes n=85	Women with diagnosed diabetes n=218	p-value
Age (years)	39.2 (0.2)	32.2 (1.1)	46.8 (0.8)	p<0.001
Race/ethnicity				p<0.001
Non-Hispanic white	72 (1)	55 (10)	61 (6)	
Non-Hispanic black	14 (1)	19 (5)	21 (3)	
Mexican-American	6 (1)	17 (4)	8 (1)	
Other	8 (1)	9 (5)	10 (3)	
Family history of diabetes	53 (2)	77 (9)	85 (3)	p<0.001
Cigarette smoking status				p=0.35
Current	31 (1)	36 (10)	27 (5)	
Former	19 (1)	10 (7)	25 (5)	
Never	51 (1)	54 (11)	48 (6)	
Alcoholic drinks per day (number)	0.44 (0.06)	0.12 (0.05)	0.03 (0.01)	p<0.001
Waist circumference (cm)	88.0 (0.41)	92.1 (3.0)	103.4 (1.8)	p<0.001
Leg length (cm)	76.4 (0.1)	75.4 (0.8)	75.7 (0.5)	p=0.18
Poverty-index-ratio (quartiles)				p=0.012
<1.49	26.0 (1.2)	27.0 (6.9)	31.3 (5.8)	
1.49 up to 2.72	26.5 (1.2)	39.4 (8.8)	30.3 (6.4)	
2.72 up to 4.20	25.3 (1.3)	26.2 (9.9)	22.8 (6.2)	
≥4.20	22.3 (1.8)	7.4 (4.9)	15.6 (5.1)	
Systolic blood pressure (mm Hg)	113.1 (0.4)	108.5 (2.1)	125.1 (2.4)	p<0.001
Diastolic blood pressure (mm Hg)	71.1 (0.3)	67.7 (1.6)	73.5 (1.1)	p=0.04
Total cholesterol (mg/dl) (fasting and non-fasting)	198.5 (1.0)	191.6 (4.0)	231.9 (5.3)	p<0.001
High density lipoprotein cholesterol (mg/dl) (fasting and non-fasting)	53.9 (0.6)	53.0 (2.0)	48.3 (1.7)	p=0.001
Urine microalbumin/creatinine (mg/g) (fasting and non-fasting)	17.0 (1.0)	22.4 (8.7)	134.0 (32.6)	p<0.001
Uric acid (mg/dl) (fasting and non-fasting)	266.2 (1.9)	262.4 (10.5)	285.9 (9.2)	p=0.029
Low-density lipoprotein cholesterol (mg/dl) *	120.6 (1.7)	113.7 (5.7)	149.8 (6.5)	p<0.001
(fasting)	n=1881	n=42	n=63	
Triglycerides (mg/dl) *	116.7 (3.0)	88.9 (8.2)	335.4 (130.6)	p=0.10
(fasting)	n=1986	n=44	n=83	
Insulin (IU/l) *	10.2 (0.3)	14.0 (1.8)	21.6 (2.6)	p<0.001
(fasting)	n=1958	n=45	n=81	
Glucose (mg/dl) *	94.0 (0.4)	106.8 (4.7)	183.9 (17.0)	p<0.001
(fasting)	n=1893	n=43	n=73	
Number of metabolic syndrome components				p=0.009
None	32 (2)	23 (12)	0 (0)	
1-2 components	50 (2)	64 (13)	14 (6)	
≥3 components	19 (2)	13 (5)	86 (6)	
Number of cardiovascular disease risk factors				p<0.001
None	30 (2)	12 (6)	0	
1-2 components	60 (2)	84 (6)	20 (6)	
≥3 components	10 (1)	4 (2)	80 (6)	

* Sample sizes differ from other laboratory tests due to the random sampling for fasting morning sample.

Table 2

Predicted probabilities and 95% confidence intervals for cardiovascular and metabolic syndrome risk factors.

	Unaffected women	Women with histories of gestational diabetes	Women with diagnosed diabetes	R ²
Systolic blood pressure (mm Hg)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	113.0 (112.5, 114.0) *	112.0 (107.4, 116.6)	120.2 (115.1, 125.3)	0.21
Model 2-further adjusted for waist circumference	113.3 (112.6, 114.0)	110.8 (105.8, 115.9)	117.4 (112.7, 122.1)	0.28
Diastolic blood pressure (mm Hg)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	71.2 (70.5, 71.9)	69.3 (65.9, 72.6)	71.3 (68.7, 73.9)	0.09
Model 2-further adjusted for waist circumference	71.3 (70.6, 71.9)	68.3 (65.7, 70.9)	69.0 (66.8, 71.2)	0.18
Total cholesterol (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	198.9 (197.0, 200.9) *	200.4 (192.3, 208.4) *	219.9 (209.0, 230.9)	0.18
Model 2-further adjusted for waist circumference	199.1 (197.1, 201.1) *	199.0 (191.3, 206.6) *	216.9 (206.6, 227.1)	0.21
HDL cholesterol (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	53.8 (52.6, 54.9) *	55.9 (52.3, 59.5) *	48.5 (45.2, 51.8)	0.09
Model 2-further adjusted for waist circumference	53.6 (52.4, 54.7)	58.0 (54.5, 61.4) *	51.6 (48.8, 54.4)	0.20
Urine microalbumin/creatinine (reference < 30 ug/g)†				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	(reference) *	1.05 (1.01, 1.08) *	0.83 (0.70, 0.97)	0.01
Model 2-further adjusted for waist circumference	(reference) *	1.05 (1.02, 1.08) *	0.85 (0.74, 0.99)	0.02
Uric acid (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	266.1 (262.3, 270.0)	268.1 (245.1, 291.2)	273.8 (252.8, 294.9)	0.05
Model 2-further adjusted for waist circumference	267.1 (263.3, 271.0)	258.1 (236.5, 279.7)	252.6 (235.6, 269.5)	0.25
LDL cholesterol (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	120.8 (117.6, 124.1) *	119.5 (106.8, 132.3)	140.2 (127.8, 152.6)	0.11
Model 2-further adjusted for waist circumference	120.9 (117.5, 124.2)	117.8 (105.9, 129.7)	138.0 (124.2, 151.7)	0.14
Triglycerides (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	116.7 (110.5, 122.9)	101.2 (78.7, 123.7)	323.0 (49.3, 596.8)	0.12
Model 2-further adjusted for waist circumference	117.3 (110.9, 123.6)	91.9 (70.7, 113.0)	314.9 (46.8, 582.9)	0.22
Fasting insulin (IU/l)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	10.2 (9.6, 10.8) *	13.0 (9.5, 16.5)	20.0 (14.6, 25.4)	0.11
Model 2-further adjusted for waist circumference	10.3 (9.7, 10.9) *	12.0 (9.2, 14.9)	18.5 (13.9, 23.2)	0.39
Fasting glucose (mg/dl)				
Model 1-adjusted for age, race, diabetes family history, smoking, alcohol	94.0 (93.2, 94.7) *	107.7 (97.7, 117.7) *	179.5 (144.2, 214.7)	0.33
Model 2-further adjusted for waist circumference	94.1 (93.3, 94.9) *	106.4 (97.3, 115.4) *	176.7 (140.6, 212.7)	0.37
Metabolic syndrome‡				
Model 1-adjusted for age, race, diabetes family history, parity, smoking, alcohol	(reference) *	0.80 (0.42, 1.51) *	3.87 (2.85, 5.26)	0.09
Model 2-not done since waist circumference already included.				
>3 Cardiovascular risk factors‡				
Model 1-adjusted for age, race, diabetes family history, parity, smoking, alcohol	(reference) *	0.69 (0.24, 1.99) *	5.19 (3.79, 7.10)	0.18
Model 2-further adjusted for waist circumference	(reference) *	0.60 (0.19, 1.85) *	4.96 (3.44, 7.13)	0.20

* Significant differences between groups are noted by lack of overlap in the 95% confidence intervals for the marginal predicted probabilities.