Published in final edited form as:

Am J Med. 2009 March ; 122(3): 207–214.e4. doi:10.1016/j.amjmed.2008.09.034.

Risk factors for type 2 diabetes among women having gestational diabetes: a systematic review

Kesha Baptiste-Roberts, PhD, MPH¹, Bethany B. Barone, ScM¹, Tiffany L. Gary, PhD, MHS^{1,4}, Sherita H. Golden, MD, MHS^{1,4}, Lisa M. Wilson, ScM⁴, Eric B. Bass, MD, MPH^{1,4}, and Wanda K. Nicholson, MD, MPH^{2,3}

¹Departments of Epidemiology, Johns Hopkins Medical Institutions, Baltimore, MD.

²Obstetrics & Gynecology, Johns Hopkins Medical Institutions, Baltimore, MD.

³Population and Family and Reproductive Health, Johns Hopkins Medical Institutions, Baltimore, MD.

⁴Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD.

Abstract

We conducted a systematic review of studies examining risk factors for the development of type 2 diabetes among women with previous gestational diabetes. Our search strategy yielded 14 articles that evaluated 9 categories of risk factors of type 2 diabetes in women with gestational diabetes: anthropometry, pregnancy-related factors, postpartum factors, parity, family history of type 2 diabetes, maternal lifestyle factors, sociodemographics, oral contraceptive use, and physiologic factors. The studies provided evidence that the risk of type 2 diabetes was significantly increased in women having increased anthropometric measures with relative measures of association ranging from 0.8 to 8.7 and women who used insulin during pregnancy with relative measures of association ranging between 2.8 and 4.7. A later gestational age at diagnosis of gestational diabetes, greater than 24 weeks gestation on average, was associated with a reduction in risk of development of type 2 diabetes with relative measures of association ranging between 0.35 to 0.99. We concluded that there is substantial evidence for three risk factors associated with the risk of type 2 diabetes in women having gestational diabetes.

Keywords

Gestational Diabetes; Type 2 Diabetes

Corresponding author: Dr. Wanda K. Nicholson, Department of Obstetrics & Gynecology, Phipps 247, 600 N. Wolfe Street, Baltimore, MD, 21205, 443-287-6942, wnichol@jhmi.edu.

Publisher's Disclaimer: Disclaimer: The authors of this article are responsible for its contents, including any clinical or treatment recommendations. No statement in this article should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

Prior Presentation: American Diabetes Association Scientific Sessions June, 2008

Introduction

Gestational diabetes, the most common medical complication of pregnancy, is defined as carbohydrate intolerance of variable degree, with an onset or first recognition occurring during pregnancy. Population-based studies estimate that gestational diabetes affects about 200,000 (7 percent) of the over 4 million births occurring annually in the United States and is associated with both maternal and neonatal complications.¹⁻³ Furthermore, the incidence of gestational diabetes doubled between the years 1994 and 2002.⁴ In 90% of women, the glucose intolerance resolves after pregnancy.⁵ Nonetheless, these women have an increased risk for later development of type 2 diabetes; 15 to 60 percent will develop type 2 diabetes mellitus within 5 to 15 years of delivery.⁶

Type 2 diabetes is a major contributor to morbidity and mortality and generates large direct and indirect costs.⁷ Therefore, the diagnosis and subsequent management of gestational diabetes after delivery has important implications for the prevention of type 2 diabetes.

There is growing interest in the effect of childbearing on the development of chronic medical conditions, including type 2 diabetes. Many studies have examined traditional risk factors for type 2 diabetes. However, no review to date has systematically examined risk factors for type 2 diabetes in women with a history of gestational diabetes or synthesized the results of published studies to establish a consensus about the most important risk factors. A review of this body of evidence could assist policymakers in the development of guidelines targeted at primary prevention of type 2 diabetes.

In this systematic review, our objective was to review the evidence on risk factors for type 2 diabetes in women with gestational diabetes, assessing the magnitude of individual risk factors and study quality and then to synthesize the results of published studies on potential risk factors for type 2 diabetes in women having gestational diabetes. The potential risk factors included sociodemographic characteristics, maternal lifestyle factors, oral contraceptive use, family history of type 2 diabetes, anthropometric measures of obesity, parity, pregnancy-related factors, and postpartum factors.

Methods

This study was part of a larger project commissioned by the Agency for Healthcare Research and Quality [AHRQ] which was conducted by the Johns Hopkins University Evidence-based Practice Center⁹ to review the literature on the association of intrapartum management and postpartum follow-up of women with gestational diabetes with maternal and neonatal outcomes.

We used a systematic approach for searching the literature. We searched four databases, MEDLINE, EMBASE, The Cochrane Central Register of Controlled Trials (CENTRAL), and the Cumulative Index to Nursing and Allied Health Literature (CINAHL), for articles published in English from inception to January 2007. Our search strategy consisted of medical subject headings (MeSH) and text words for gestational diabetes, type 2 diabetes, and other terms relevant to the other questions (see Appendix A for full text of search string). We hand searched the table of contents of recent issues of 13 journals (See Appendix

B) that were most likely to publish articles on this topic. We also checked the references in included articles and other pertinent reviews.

Study Selection

Two reviewers independently reviewed all citations for inclusion. Articles were excluded if both investigators agreed that the article met one or more of the following exclusion criteria: 1) not written in English; 2) did not include any human data; 3) contained no original data (i.e., was a meeting abstract, editorial, commentary, or letter); 4) less than 90% of the sample was diagnosed with gestational diabetes there was no separate analysis for mothers with gestational diabetes; 5) was a case report or case series; 6) did not base the diagnosis of gestational diabetes on either a 3-hour, 100-gm oral glucose tolerance test or a 2-hour, 75-gm oral glucose tolerance test; 7) did not evaluate the development of type 2 diabetes (diagnosed by fasting blood glucose (FBG) greater than 125 mg/dL, 75-gm oral glucose tolerance test 2-hr glucose greater than 200 mg/dL, random blood glucose greater than 200 mg/dL, self-reported type 2 diabetes, or current use of an anti-diabetic medication); or 8) there was neither a relative measure of association nor incidence reported. Differences of opinion regarding abstract eligibility were resolved through consensus adjudication.

Data Abstraction

Two reviewers sequentially abstracted information from each article using standardized data abstraction forms. Reviewers were not masked to the articles' authors, institutions, or journal.¹⁰

Study Quality Assessment

Two reviewers independently assessed study quality using items from the Strengthening the reporting of observational epidemiological studies [STROBE] checklist for the reporting of observational studies.¹¹ The STROBE checklist includes items on the statement of hypotheses, eligibility criteria, study population, power and sample size calculations, definition of outcomes, loss to follow-up, and missing data.

Rating the Body of Evidence

We used the evidence grading scheme recommended by the Grading of Recommendations Assessment Development and Evaluation [GRADE] Working Group¹² to grade the quantity, quality, and consistency of the best available evidence as high, moderate, low, very low, or insufficient.

Results

Search Results

From the general search for the primary literature review, we retrieved 11,400 unique citations. After reviewing titles and abstracts, 551 were eligible for further review. After excluding 538 that did not meet eligibility criteria for this question, 14 articles were identified for review that evaluated potential risk factors for developing type 2 diabetes in women with prior gestational diabetes (Table 1).

Study Characteristics

The studies were conducted in diverse populations and included 10 studies in North America, three studies in Asia, two studies in Europe, and one study in Australia. Patients were recruited from a hospital or hospital-based clinic for all studies. The follow-up time for the studies ranged from 6 weeks to 12 years (see Table 1).

Study Quality

Studies varied with respect to their quality (see Table 2). Each of the 14 studies reported eligibility criteria and most studies reported how the outcome of type 2 diabetes was defined (93.3 percent). Seventy five percent of studies reported the loss to follow-up rate, with 75 percent of those having a loss to follow-up of greater than 20 percent. None of the studies reported power or sample size calculations or strategies applied to handle missing data. Studies varied in their reporting of baseline characteristics of participants (see Table 1).

Our systematic review yielded the most evidence for three risk factors: measures of anthropometry, gestational age at diagnosis of gestational diabetes, and method of glucose control.

Measures of anthropometry

We identified 11 cohort studies that evaluated a total of 11 different anthropometric measures (see Figure 1).^{13–23} Anthropometric measures included weight, height, BMI, body fat weight, subscapular skin fold thickness, suprailiac skin fold thickness, tricep skin fold thickness, waist circumference, waist-to-hip ratio, percent ideal body weight, and weight change. Of the 11 studies, 9 reported a relative measure of association.^{13–17;19–22}

Of the 11 studies, three evaluated pre-pregnancy anthropometric measures. Three studies evaluated pre-pregnancy BMI^{14;17;21} and one study also evaluated pre-pregnancy weight.¹⁷ Two of these studies reported a significant positive association between pre-pregnancy BMI²¹ and pre-pregnancy weight¹⁷ and the development of type 2 diabetes respectively, one study found no association¹⁴ and one study did not report the measure of association (see Figure 1).¹⁷ Pallardo et al. found that as compared to women with a pre-pregnancy BMI less than or equal to 27 kg/m², women with a BMI greater than 27 kg/m² had an eight-fold increased risk of developing type 2 diabetes, after adjustment for the number of abnormal glucose results from the OGTT and C-peptide glucose score (Odds Ratio [OR] = 8.7; 95 percent Confidence Interval [CI]: 2.3 to 32.9)²¹. Jang et al. reported that for every 1-kg increase in pre-pregnancy weight, there was a 40 percent increase in the odds of developing type 2 diabetes (OR = 1.40.(CI: 1.20 to 1.60).¹⁷

Three of the 11 studies evaluated anthropometric measures during pregnancy and reported a positive association after adjustment (See Figure 1).^{13;19;20} Four studies^{15;16;22;23} evaluated anthropometric measures assessed during the postpartum period. As shown in Figure 1, Cho et al. assessed seven anthropometric measures, comparing women in the highest quartile to those in the lowest quartile¹⁵. Each of the seven measures was positively associated with the development of type 2 diabetes, after adjustment for age, duration of follow-up, parity, family history of type 2 diabetes, working status, blood pressure, and lipid profile. The

direction and magnitude of the association with type 2 diabetes were similar across several additional anthropometric measures. Two additional studies assessed postpartum BMI^{22;23} and postpartum weight²³ in multivariate models but did not report the strength nor the significance of the association. In an unadjusted analysis, Dacus et al. reported a four-fold increased risk (RR = 4.1; 95 percent CI: 0.6 – 29.8) in the development of type 2 diabetes among women with a postpartum BMI of 27 kg/m² or greater compared to women with a postpartum BMI less than 27 kg/m².¹⁶

Three studies evaluated anthropometric measures as time-dependent covariates, assessing the association of the change in these measures between delivery and follow-up and the development of type 2 diabetes^{18;22;23}. Peters et al. reported that for every 10-pound change in weight, there was a 2-fold increase in the risk of developing type 2 diabetes, after adjusting for additional pregnancy, OGTT glucose area, postpartum BMI, and breastfeeding.²² Although Kjos et al. and Xiang et al. included weight change in the multivariate analysis, the relative association of weight change with type 2 diabetes was not reported.^{18;23} Height was examined in one study, but the measure of association from the multivariate model was not reported.¹⁷

Gestational age at diagnosis of gestational diabetes

Five studies^{14;16;17;24;25} assessed gestational age at diagnosis of gestational diabetes as a risk factor (see Figure 2), and four of the five studies used multivariate analysis.^{14;17;24;25} The studies varied in terms of their categorization of gestational age at gestational diabetes diagnosis. Both Kjos et al.²⁴ and Schaefer-Graf et al.²⁵ reported a reduction in the likelihood of developing type 2 diabetes associated with a gestational age at gestational diabetes diagnosis in the fourth quartile as compared to the first quartile. Both studies varied with respect to the covariates included in the multivariate model sharing no common covariates. When gestational age at gestational diabetes diagnosis in the third quartile was compared to the first quartile, a smaller effect was observed in both studies. For both studies, when gestational age at gestational diabetes diagnosis in the second quartile was compared to the first quartile, the authors reported no significant difference in the development of type 2 diabetes.

Jang et al. assessed gestational age at gestational diabetes diagnosis as a continuous variable and found that for each week of increase in gestational age at gestational diabetes diagnosis, there was a 0.99 decrease in the odds of developing type 2 diabetes.¹⁷ In two studies, the results were not statistically significant.^{14;16}

Method of glucose control

Five studies evaluated the method of glucose control during pregnancy as a risk factor for the development of type 2 diabetes.^{13;16;18;19;26} Only three of these studies reported a relative measure of association (Figure 3). Three studies^{13;18;19} included a multivariate analysis, but only two^{13;19} reported a relative measure of association for this risk factor (Figure 3). Cheung et al. reported that compared to women who did not use insulin, those that used insulin during pregnancy had a three-fold higher risk of developing type 2 diabetes after adjusting for age, parity, FBG at diagnosis, BMI at index pregnancy, 2-hr oral glucose

tolerance test, number of prior pregnancies complicated by gestational diabetes, family history of type 2 diabetes, and hospital location (RR = 3.2; 95 percent CI: 1.6 to 7.0).¹³ Lobner et al. reported that compared to women who were diet-controlled, women who received insulin during pregnancy had an almost five-fold increased risk of developing type 2 diabetes after adjustment for age, parity, GAD and IA-2 antibody status, BMI during pregnancy, and serum CRP (RH = 4.7; 95 percent CI: 3.2 to 7.1; $p < 0.0001$).¹⁹

Two studies were identified that conducted a univariate analysis^{16;26}, but only Steinhart et al. reported a relative measure of association indicating no statistically significant relationship.²⁶

Summary of data on other risk factors for Type 2 Diabetes

Several additional risk factors were evaluated and as a result of the limited number of studies, sparseness of data and limited number of reported relative associations, we chose to describe the results qualitatively in Table 3.

Grading the body of evidence

Because of multiple cohort studies and measures of association, we graded the overall evidence for anthropometric measures and pregnancy-related factors as moderate. We concluded that the overall grade of the evidence for postpartum factors was very low.

Discussion

In this systematic review, we found substantial and consistent evidence that anthropometric measures of obesity, gestational age at gestational diabetes diagnosis, and method of glucose control were risk factors for the subsequent development of type 2 diabetes among women with previous gestational diabetes. The evidence was too weak to draw firm conclusions about other risk factors. No evidence on maternal lifestyle factors and risk of type 2 diabetes was found in this review, suggesting that this area is understudied.

The literature itself was heterogeneous with respect to the ethnic populations sampled, risk factors considered, and methods of statistical analysis. While a multivariate analytic approach was used to evaluate most of the risk factors for the development of type 2 diabetes, the factors considered and adjusted for in the multivariate models differed between studies. For example, some studies focused on anthropometry while others focused on a broader range of potential risk factors. Results of both univariate and multivariate analyses were complicated by differences in how risk factors were defined and covariates included in the multivariate analyses. Some studies determined which variable to include in the multivariate models by identifying the most significant predictors from the univariate analysis or taking a stepwise modeling approach. Other studies did not report how or why specific covariates were chosen to be included in the models. Most studies included a list of key covariates known to be associated with type 2 diabetes risk, including age, parity, family history of type 2 diabetes, and method of glucose control (diet versus insulin or oral medication). Age was included in all of the multivariate models. However, no one study included all of the other three key covariates. Also, no group of covariates was common to all of the multivariate models constructed for the evaluation of a given risk factor.

Our systematic review highlights important weaknesses in the literature. We did not find any study that included maternal lifestyle factors in its evaluation of risk factors for the development of type 2 diabetes. It is also unclear as to what extent selection bias might have influenced the results since all of the studies in this review were based on convenience sampling. Random or purposeful sampling of participants would yield a more representative group of participants. Our analysis also reveals the paucity of independent, methodologically rigorous studies that examine risk factors for the development of type 2 diabetes among women with previous gestational diabetes.

It is possible that we did not identify all of the relevant studies on this topic given that search strategies are not as well developed for finding risk factor studies as for trials of therapeutic interventions. However, we employed a comprehensive process of literature identification that should identify the most important studies. Second, there is the possibility of publication bias where studies with significant associations are more likely to be published than studies without significant associations, but we did find a number of studies reporting insignificant associations. Third, we excluded all studies which did not base the diagnosis of gestational diabetes on either a 3-hour, 100-gm oral glucose tolerance test or a 2-hour, 75-gm oral glucose tolerance test, thereby excluding studies that relied on self-reported gestational diabetes. Although this excludes some evidence, we contend that such evidence would be very weak. Fourth, we were unable to perform meta-analyses for summary risk measures because of the heterogeneity of the risk factors examined in each study. Finally, study quality varied for different risk factors ranging from very low to moderate.

This review has several implications for clinical practice and future research. First, obstetricians and primary care providers can use the results of antepartum and postpartum tests from women with prior gestational diabetes to identify those at highest risk for type 2 diabetes, who would most benefit from targeted interventions to prevent the disease. The Diabetes Prevention Program [DPP] found that lifestyle and pharmacologic interventions were both successful in delaying diabetes among women with a history of gestational diabetes²⁷. The Troglitazone in Prevention of Diabetes [TRIPOD]²⁸ and the Pioglitazone in Prevention of Diabetes [PIPOD]²⁹ demonstrated that pharmacologic intervention may preserve beta-cell function among women with a recent history of gestational diabetes.

Second, the current level of postpartum screening following an index gestational diabetes pregnancy is suboptimal and needs to be more widespread.^{30;31} These levels need to be increased to ensure appropriate follow-up of women at risk for type 2 diabetes. Clinicians could develop better interdisciplinary collaborations for ongoing care following a pregnancy with gestational diabetes. Specifically, clinicians providing prenatal and obstetrical care might link their gestational diabetes patients with an internist or family practitioner during the course of pregnancy to ensure on-going continuity of care after delivery.

Finally, studies are needed to explore the effect of maternal lifestyle factors and the development of type 2 diabetes among women with previous gestational diabetes. Tailoring of interventions based on the success of DPP to women with gestational diabetes might alter maternal lifestyle behaviors, thereby improving their future post-reproductive health profile. In addition, women may be responsive to implementing preventive interventions to reduce

adiposity to improve their fetus' health even more than their own, as suggested by the high rates of smoking cessation rates during pregnancy.³² Pregnancy might provide an optimal time for targeted interventions for lifestyle modifications among women known to be at high risk for developing type 2 diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Source: Agency for Healthcare Research and Quality

References

1. Ferrara A, Hedderston MM, Quesenberry CP, Selby JV. Prevalence of gestational diabetes mellitus detected by the national diabetes data group or the carpenter and coustan plasma glucose thresholds. *Diabetes Care* 2002;25:1625–30. [PubMed: 12196438]
2. Hunt KJ, Schuller KL. The increasing prevalence of diabetes in pregnancy. *Obstet.Gynecol.Clin.North Am.* 2007;34:173–99, vii. [PubMed: 17572266]
3. Rosenberg TJ, Garbers S, Lipkind H, Chiasson MA. Maternal obesity and diabetes as risk factors for adverse pregnancy outcomes: differences among 4 racial/ethnic groups. *Am.J Public Health* 2005;95:1545–51. [PubMed: 16118366]
4. Dabelea D, Snell-Bergeon JK, Hartsfield CL, Bischoff KJ, Hamman RF, McDuffie RS. Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort: Kaiser Permanente of Colorado GDM Screening Program. *Diabetes Care* 2005;28:579–84. [PubMed: 15735191]
5. Kjos SL, Buchanan TA, Greenspoon JS, Montoro M, Bernstein GS, Mestman JH. Gestational diabetes mellitus: the prevalence of glucose intolerance and diabetes mellitus in the first two months post partum. *Am.J.Obstet.Gynecol.* 1990;163:93–98. [PubMed: 2375376]
6. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002;25:1862–68. [PubMed: 12351492]
7. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998;21:1414–31. [PubMed: 9727886]
8. Gary TL, Brancati FL. Strategies to curb the epidemic of diabetes and obesity in primary care settings. *J Gen.Intern.Med* 2004;19:1242–43. [PubMed: 15610336]
9. Nicholson WK, Wilson LM, Witkop CT, Baptiste-Roberts K, Bennett WK, Bolen S, Barone BB, Golden SH, Gary TL, Neale DM, and Bass EB Therapeutic Management, Delivery, and Postpartum Risk Assessment and Screening in Gestational Diabetes. 08–E004. 2008.
10. Berlin JA. Does blinding of readers affect the results of meta-analyses? University of Pennsylvania Meta-analysis Blinding Study Group. *Lancet* 1997;350:185–86.
11. Altman D, Egger M, Pocock S, Vandenbrouke JP, and von Elm E Strengthening the reporting of observational epidemiological studies. STROBE Statement: Checklist of Essential Items Version 3. 2005.
12. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328:1490. [PubMed: 15205295]
13. Cheung NW, Helmsink D. Gestational diabetes: the significance of persistent fasting hyperglycemia for the subsequent development of diabetes mellitus. *J Diabetes Complications* 2006;20:21–5. [PubMed: 16389163]
14. Cho NH, Lim S, Jang HC, Park HK, Metzger BE. Elevated homocysteine as a risk factor for the development of diabetes in women with a previous history of gestational diabetes mellitus: a 4-year prospective study. *Diabetes Care* 2005;28:2750–5. [PubMed: 16249551]

15. Cho NH, Jang HC, Park HK, Cho YW. Waist circumference is the key risk factor for diabetes in Korean women with history of gestational diabetes. *Diabetes Res Clin Pract* 2006;71:177–83. [PubMed: 16054264]
16. Dacus JV, Meyer NL, Muram D, Stilson R, Phipps P, Sibai BM. Gestational diabetes: postpartum glucose tolerance testing. *Am J Obstet Gynecol* 1994;171:927–31. [PubMed: 7943102]
17. Jang HC, Yim CH, Han KO, Yoon HK, Han IK, Kim MY et al. Gestational diabetes mellitus in Korea: prevalence and prediction of glucose intolerance at early postpartum. *Diabetes Res Clin Pract* 2003;61:117–24. [PubMed: 12951280]
18. Kjos SL, Peters RK, Xiang A, Thomas D, Schaefer U, Buchanan TA. Contraception and the risk of type 2 diabetes mellitus in Latina women with prior gestational diabetes mellitus. *JAMA* 1998;280:533–8. [PubMed: 9707143]
19. Lobner K, Knopff A, Baumgarten A, Mollenhauer U, Marienfeld S, Garrido-Franco M et al. Predictors of postpartum diabetes in women with gestational diabetes mellitus. *Diabetes* 2006;55:792–7. [PubMed: 16505245]
20. Metzger BE, Cho NH, Roston SM, Radvany R. Prepregnancy weight and antepartum insulin secretion predict glucose tolerance five years after gestational diabetes mellitus. *Diabetes Care* 1993;16:1598–605. [PubMed: 8299456]
21. Pallardo F, Herranz L, Garcia-Ingelmo T, Grande C, Martin-Vaquero P, Janez M et al. Early postpartum metabolic assessment in women with prior gestational diabetes. *Diabetes Care* 1999;22:1053–8. [PubMed: 10388966]
22. Peters RK, Kjos SL, Xiang A, Buchanan TA. Long-term diabetogenic effect of single pregnancy in women with previous gestational diabetes mellitus. *Lancet* 1996;347:227–30. [PubMed: 8551882]
23. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA. Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. *Diabetes Care* 2006;29:613–7. [PubMed: 16505515]
24. Kjos SL, Peters RK, Xiang A, Henry OA, Montoro M, Buchanan TA. Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum glucose tolerance testing. *Diabetes* 1995;44:586–91. [PubMed: 7729620]
25. Schaefer-Graf UM, Buchanan TA, Xiang AH, Peters RK, Kjos SL. Clinical predictors for a high risk for the development of diabetes mellitus in the early puerperium in women with recent gestational diabetes mellitus. *Am J Obstet Gynecol* 2002;186:751–6. [PubMed: 11967502]
26. Steinhart JR, Sugarman JR, Connell FA. Gestational diabetes is a herald of NIDDM in Navajo women. High rate of abnormal glucose tolerance after GDM. *Diabetes Care* 1997;20:943–7. [PubMed: 9167104]
27. Ratner R. Women with a history of gestational diabetes in the Diabetes Prevention Program; Chicago IL. Fourth International Workshop-Conference on Gestational Diabetes Mellitus; 2005. 2005
28. Buchanan TA, Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk hispanic women. *Diabetes* 2002;51:2796–803. [PubMed: 12196473]
29. Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, Ochoa C et al. Effect of pioglitazone on pancreatic beta-cell function and diabetes risk in Hispanic women with prior gestational diabetes. *Diabetes* 2006;55:517–22. [PubMed: 16443789]
30. Kim C, Tabaei BP, Burke R, McEwen LN, Lash RW, Johnson SL et al. Missed opportunities for type 2 diabetes mellitus screening among women with a history of gestational diabetes mellitus. *Am.J Public Health* 2006;96:1643–48. [PubMed: 16873752]
31. Smirnakis KV, Chasan-Taber L, Wolf M, Markenson G, Ecker JL, Thadhani R. Postpartum diabetes screening in women with a history of gestational diabetes. *Obstet.Gynecol.* 2005;106:1297–303. [PubMed: 16319255]
32. O'Campo P, Faden RR, Brown H, Gielen AC. The impact of pregnancy on women's prenatal and postpartum smoking behavior. *Am.J Prev.Med* 1992;8:8–13. [PubMed: 1576004]

Figure 1. Summary of reported measures of association between measures of anthropometry and the risk of developing type 2 diabetes following a pregnancy with gestational diabetes mellitus

* Comparison is between the highest and the lowest quartile. BMI = body mass index; kg = kilograms; m = meters; OR = odds ratio; PIBW = percent of ideal body weight; Q = quartile; RH = relative hazard; RR = relative risk

Figure 2. Summary of reported measures of association between gestational age at diagnosis of gestational diabetes mellitus and the risk of developing type 2 diabetes following a pregnancy with gestational diabetes mellitus

OR = odds ratio; Q = quartile; RH = relative hazard; RR = relative risk

Figure 3. Summary of reported measures of association between method of glucose control and the risk of developing type 2 diabetes following a pregnancy with gestational diabetes mellitus
OR = odds ratio; RH = relative hazard; RR = relative risk

Characteristics of studies reporting on the risk associated with the development of type 2 diabetes mellitus following a pregnancy with gestational diabetes (continued)

Table 1.

Author, year Country Study design	Age (in years), mean	Race, n (%)	Gravida and parity, mean	N	Diabetes diagnosis	Followup time	Covariates considered
Cheung, 2006 ¹³ Australia Cohort	ND: 32.3 T2DM: 31.9 T: 32.1	NR	ND: parity: 1.6 T2DM: parity: 0.9 T: parity: 1.4	102	Abnormal 75-gm OGTT, self report followed by verification from local doctor or abnormal 75-gm OGTT at retest	0–8 years, mean=4.5 years	Age, parity, FPG at diagnosis, BMI at index pregnancy, 2-hr OGTT, # prior GDM pregnancies, method of glucose control, FHxT2DM, hospital, fasting blood glucose level, dose of bedtime intermediate-acting insulin required
Cho, 2005 ¹⁴ Korea Cohort	NGT: 30.6 IGT: 32.1 T2DM: 30	NR	NGT: (3 children (%): 32.1) IGT: (3 children (%): 55.8) T2DM: (3 children (%): 33.3)	170	Abnormal 75-gm OGTT	6 weeks and annually thereafter	Age, pre-pregnancy BMI, parity, method of glucose control, gestational age at GDM diagnosis, FHxT2DM, FPG at diagnosis, homocysteine level
Cho, 2006 ¹⁵ Korea Cohort	NGT: 33.2 IGT: 34.2 T2DM: 33	NR	NGT: (para 1 (%): 39.0; para 2 (%): 51.4; para 3+ (%): 9.5) IGT: (para 1 (%): 37.8; para 2 (%): 56.9; para 3+ (%): 3.4) T2DM: (para 1 (%): 39.7; para 2 (%): 56.9; para 3+ (%): 3.4)	909	Abnormal 75-gm OGTT	6 weeks, annually up to 6 years	Age, parity, body fat %, total cholesterol, triglycerides, postpartum BMI, blood pressure, lipid profile, * duration of followup, FHxT2DM, working status, postpartum waist circumference, postpartum weight, postpartum subscapular skin fold thickness, postpartum suprailiac skin fold thickness, postpartum tricep skin fold thickness, postpartum body fat weight, postpartum waist-to-hip ratio
Dacus, 1994 ¹⁶ US Cohort	ND: 30 year (n, %): 40 (47%); <30 year (n, %): 46 (53%) T2DM: 30 year (n, %): 5 (36%); <30 year (n, %): 9 (64%)	ND: AA: 60 (70); C: 23 (27); Other: 3 (3) T2DM: AA: 11 (72); C: 2 (21); Other: 1 (7)	NR	100	Abnormal 75-gm OGTT	5–10 weeks postpartum	Age, race, gestational age at GDM diagnosis, method of glucose control, postpartum BMI
Jang, 2003 ¹⁷ Korea Cohort	T: 30.9	T: NR	T: parity: 0.5	311	Abnormal 75-gm OGTT	NR	Age, pre-pregnancy weight, pre-pregnancy BMI, parity, gestational age at delivery,

Author, year Country Study design	Age (in years), mean	Race, n (%)	Gravida and parity, mean	N	Diabetes diagnosis	Followup time	Covariates considered
Kjos, 1995 ²⁴ US Cohort	T: 30.3	T: Hisp: 671 (100)	T: parity: 2.8	671	Abnormal 75-gm OGTT	Between 4 to 16 weeks; Additional followup within 7.5 years postpartum	GDM class A1, gestational age at GDM diagnosis, 2-hr glucose, 3-hr insulin on diagnostic OGTT, height, FHxT2DM, postpartum weight
Kjos, 1998 ¹⁸ US Cohort	COC: 28.5 Progestin only: 29.4	COC: Hisp: 383 (100) Progestin only: Hisp: 78 (100)	COC: parity: 2.3 Progestin only: parity: 3.1	443	Abnormal 75-gm OGTT	Varied (Cox model)	Age, race, postpartum BMI, parity, method of glucose control, total cholesterol, mean arterial pressure, postpartum FPG, contraceptive use, AUC at the initial postpartum OGTT, prior OC use, additional pregnancy, postpartum weight change, duration of OC use
Lobner, 2006 ¹⁹ Germany Cohort	Autoantibody (+): 29.9 Autoantibody (-): 31.4 T: NR	NR	NR	302	Abnormal 75-gm OGTT	9 months and 2, 5, 8 and 11 years postpartum	Age, BMI at first pregnancy visit, method of glucose control, HLA DR3 or DR4- DQ8, 8-year DM risk (%), GAD and IA-2 antibody status, parity, serum CRP
Metzger, 1993 ²⁰ US Cohort	Model 1 ND: 31.7 IGT: 32.0 T2DM: 33.0 Model 2 ND: 31.4 IGT: 31.7 T2DM: 32.3	NR	Model 1: parity ND: 1.5 IGT: 1.5 T2DM: 1.7 Model 2: parity ND: 1.6 IGT: 1.3 T2DM: 2.1	Model 1 177 Model 2 172	Abnormal 100-gm OGTT	3–6 months (model 1), and year 1,2,3,4,&5 (model 2)	Age, race, FHxT2DM, parity, obesity, basal glucose, basal insulin, 2-hr glucose, 3-hr integrated insulin, OGTT 30- min stimulated insulin secretion
Pallardo, 1999 ²¹ Spain Cohort	ND: 33.1 T2DM: 32.6	ND: C: 745 (100) T2DM: C: 43 (100)	ND: parity: 1.89 T2DM: parity: 1.94	788	Abnormal 75-gm OGTT	3–6 months	Age, race, parity, pre-pregnancy BMI, recurrence of GDM, FHxT2DM, # of abnormal OGTT results (including fasting), C-peptide glucose score
Peters, 1996 ²² US Cohort	No additional pregnancy: 30.4 Additional pregnancy: 29.9	No additional pregnancy: Hisp: 578 (100) Additional pregnancy:	No additional pregnancy: parity: 2.8 Additional pregnancy: parity: 2.8	666	Abnormal 75-gm OGTT	3–89 months	Age, race, parity, gestational age at delivery, duration of followup, oral contraceptive use, additional pregnancy, postpartum weight change, OGTT glucose area, postpartum BMI, breastfeeding

Author, year Country Study design	Age (in years), mean	Race, n (%)	Gravida and parity, mean	N	Diabetes diagnosis	Followup time	Covariates considered
Hispanic: 87 (100)							
Schaefer-Graf, 2002 ²⁵ US Cohort	ND: 31.1 T2DM: 32.2 T: 31.2	NR	ND: parity: 1.9 T2DM: parity: 2.2 T: NR	1636	Abnormal 75-gm OGTT, taking diabetes medications	1–4 months	Age, parity, previous macrosomia, previous stillbirth, FPG at diagnosis, class A2, area under the glucose curve of pregnancy OGTT, gestational age at GDM diagnosis, previous GDM, 50-gm GCT
Steinhart, 1997 ²⁶ US Cohort	ND: 31 NIDDM: 32.7	ND: American Indian: 41 NIDDM: American Indian: 47	ND: parity: 2.45 NIDDM: parity: 3.43	88	Abnormal 75-gm OGTT, type 2 diabetes diagnosed in medical record	9–12 years	Age, race, parity, BMI at GTT, fasting blood sugar, spontaneous abortions, GTT total, recurrent GDM, method of glucose control
Xiang, 2006 ¹⁹ US Cohort	DMPA: 30 COC: 29	DMPA: Hispanic: 96 (100) COC: Hispanic: 430 (100)	DMPA: parity: 2.6 COC: parity: 2.3	526	Abnormal 75-gm OGTT	4–6 weeks, 3–6 month intervals thereafter	Age, race, parity, method of glucose control, contraceptive use, postpartum BMI, breastfeeding, FHxT2DM, HDL cholesterol, triglycerides, weight change during followup, interaction term for OC use and triglyceride level, interaction term for breastfeeding and OC use

* Includes triglyceride, high density lipoprotein, and low density lipoprotein cholesterol.

AA = African American; AUC = area under the curve; BMI = body mass index; C = Caucasian; COC = combination oral contraceptive; CRP = C-reactive protein; DMPA = depomedroxyprogesterone acetate; FPG = fasting plasma glucose; FSIGT = frequently sampled intravenous glucose tolerance; GAD = glutamic acid decarboxylase; GCT = glucose challenge test; GDM = gestational diabetes mellitus; gm = gram; GTT = glucose tolerance test; HDL = high density lipoprotein; Hisp = Hispanic; HLA = human leukocyte antigen-2; IGT = impaired glucose tolerance; min = minutes; ND = non-diabetic; NGT = normal glucose tolerance; NIDDM = non-insulin dependent diabetes mellitus; NR = not reported; OC = oral contraceptive; OGTT = oral glucose tolerance test; SI = sensitivity index; T2DM = type 2 diabetes mellitus; T = total; US = United States

Quality of studies reporting on the risk associated with the development of type 2 diabetes following a pregnancy with gestational diabetes

Table 2.

Author, year	Are pre-specified hypotheses stated?	Are inclusion and exclusion criteria reported?	Sampling	Were power or sample size calculations used?	Does the article state how the outcome was defined?	Loss to followup / Report comparisons of those lost to followup vs participants	Percent of missing data / Report how missing data was handled
Cheung, 2006	●	●	Convenience		●	>20% / ●	
Cho, 2005		●	Convenience		●	>20% /	
Cho, 2006		●	Convenience		●	>20% /	
Dacus, 1994	●	●	Convenience		●	>20% /	
Jang, 2003	●	●	Convenience		●	10–20% / ●	
Kjos, 1995	●	●	Convenience		●	>20% /	
Kjos, 1998		●	Consecutive		●		
Lobner, 2006	●	●	Convenience		●	>20% /	
Metzger, 1993			Convenience		●	>20% /	
Pallardo, 1999	●	●	Convenience		●	>20% / ●	
Peters, 1996		●	Consecutive		●		
Schaefer-Graf, 2002	●	●	Convenience		●	>20% / ●	10–20% /
Steinhart, 1997		●	Consecutive		●	>20% /	
Xiang, 2006		●	Convenience				

Table 3.

Summary of the evidence of the association between selected potential risk factors and the development of type 2 diabetes mellitus following a pregnancy with gestational diabetes

Risk Factor	Number of studies	Number of studies reporting a relative measure of association	Measure of Association (95% CI)	Covariates considered
Family History of type 2 diabetes	5	1	No: ref Yes: RR = 1.706 (0.638 – 4.566)	Age, gestational age at GDM diagnosis, pre-pregnancy BMI, FPG at diagnosis, homocysteine level
Age	6	2	30: ref >30: RR = 2.03 (0.682 – 6.03)	Gestational age at GDM diagnosis, pre-pregnancy BMI, FHxT2DM, FPG at diagnosis, homocysteine level;
			<30: ref 30: RR = 0.68 (0.24 – 1.88)	No covariates
Race	1	1	Other: ref Black: RR=1.5 (0.45 – 4.98)	No covariates
Parity	4	2	0: ref 1-2: RH = 1.2 (0.8 – 1.7; p = 0.45) >2: RH = 2.5 (1.1 – 5.3; p = 0.02)	GAD and IA-2 antibody status, method of glucose control, BMI at first pregnancy visit, age, serum CRP;
			OR = 1.21 (p = 0.09)	3-hr integrated insulin, obesity
Dosage of bedtime insulin	1	1	RR = 1.1 91.0 – 1.2)	FBG
50-gm GCT	1	1	Q1: ref Q2: OR = 2.86 (1.24 – 6.58) Q3: OR = 3.82 (1.72 – 8.48) Q4: OR = 3.46 (1.57 – 7.64)	FPG at diagnosis, class A2, area under the glucose curve of pregnancy OGTT, gestational age at GDM diagnosis, previous GDM
Class A-2	1	1	No: ref Yes: OR = 2.4 (1.22 – 4.72)	FPG at diagnosis, area under the glucose curve of pregnancy OGTT, gestational age at GDM diagnosis, previous GDM, 50-g GCT
Previous pregnancy complicated by GDM	2	1	No: ref Yes: OR = 1.63 (1.07 – 2.47)	FPG at diagnosis, area under the glucose curve of pregnancy OGTT, gestational age at GDM diagnosis, previous GDM, 50-g GCT
Spontaneous abortion	1	1	No: ref Spontaneous abortion: OR = 1.36 (0.5 – 3.5)	No covariates
Postpartum factors				
Additional Pregnancy	2	1	No: ref Yes: RH = 3.34 (1.8 – 6.19)	Postpartum weight change, OGTT glucose area, postpartum BMI, breastfeeding
Breastfeeding	2	0		
Duration of follow up	1	0		

Risk Factor	Number of studies	Number of studies reporting a relative measure of association	Measure of Association (95% CI)	Covariates considered
Recurrent gestational diabetes	1	1	No recurrent GDM: ref Recurrent GDM: OR= 24.8 (3 – 1132.2)	
Oral Contraceptive	2	2	Combination therapy: ref Progestin only: RH = 2.87 (1.57 – 5.27)	Area under the glucose curve at the initial postpartum OGTT, prior OC use, method of glucose control, additional pregnancy, postpartum weight loss, duration of OC use;
			COC use: ref DMPA use: RH = 1.07 (0.61 – 1.89)	Postpartum BMI, breastfeeding, FHxT2DM, HDL cholesterol, triglycerides, weight change during follow-up
Duration of contraceptive use	1	1	4: RH = 0.72 (0.09 – 5.89) 4–8: RH = 2.96 (1.35 – 6.52) >8: RH = 4.92 (1.76 – 13.73)	Contraceptive use, AUC at the initial postpartum OGTT, prior OC use, method of glucose control, additional pregnancy, postpartum weight loss

BMI = body mass index; CI = confidence interval; class A2 = insulin-requiring gestational diabetes; CRP = C = reactive protein;; FHxT2DM = family history of type 2 diabetes mellitus; FPG = fasting plasma glucose; GAD = glutamic acid decarboxylase; GDM = gestational diabetes mellitus; gm = grams; GCT = glucose challenge test; HDL = high density lipoprotein; OC = oral contraceptive; OGTT = oral glucose tolerance test; OR = odds ratio; ref = reference; Q = quartile; RH = relative hazard; RR = relative risk; se = standard error; SI = sensitivity index