Review
Epidemiology

Diabetes Metab J 2014;38:1-12
http://dx.doi.org/10.4093/dmj.2014.38.1.1
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

Gestational Diabetes Mellitus in Korean Women: Similarities and Differences from Other Racial/Ethnic Groups

Catherine Kim[1,2]

Departments of [1]Medicine, [2]Obstetrics and Gynecology, University of Michigan Medical School, Ann Arbor, MI, USA

Gestational diabetes mellitus (GDM) reflects defects in insulin secretion in response to the metabolic demands of pregnancy. While GDM is increasingly common worldwide due in large part to the obesity epidemic, its frequency is relatively low in Korean women. In this report, the prevalence and risk factors for GDM, perinatal outcomes, and postpartum course are compared in non-Korean and Korean women. While Koreans and non-Koreans with GDM share pathophysiology and complications, there may be differences in the role of obesity and thus the effectiveness of interventions targeting obesity in GDM women. Further investigations of the effectiveness of weight loss interventions and pharmacotherapy specifically among Korean women are needed. Dietary and other lifestyle data from Korean populations could inform prevention and treatment strategies in other countries which suffer from significantly higher prevalences of GDM.

Keywords: Diabetes, gestational; Epidemiology; Postpartum period; Pregnancy

INTRODUCTION

Gestational diabetes mellitus (GDM) is a disease state characterized by underlying defects in maternal insulin sensitivity and secretion, which are unmasked in response to the metabolic stressors of pregnancy [1]. In this review, I summarize what is known about the epidemiology of GDM among Korean women and discuss similarities and differences with reports from other countries. First, I review prevalence of GDM and risk factors, particularly body mass index (BMI) and the genetics of GDM. Second, I discuss perinatal outcomes, specifically macrosomia. I conclude with a discussion of postpartum maternal outcomes and behavior modification.

PREVALENCE AND RISK FACTORS FOR GDM

Due to increases in prepregnancy maternal body weight and increasing gestational weight gain [2], the United States and other countries have observed increases in the prevalence of GDM over the past few decades [3,4]. These increases have occurred independent of changes in diagnostic criteria. As population-based trend data are not available, it is not known if Korean women have experienced similar increases in GDM prevalence, prepregnancy weight, or gestational weight gain over the past 20 years. However, hospital-based reports suggest that the prepregnancy BMI of Korean mothers has not changed substantially in the past two decades [5,6]. In 1995, the prevalence of GDM in Korea was only 2% in Korea [5]. This estimate is similar to a report including ethnic Korean women living in the United States in 2003 [7]. In this report, using a national birth-certificate based dataset maintained by the Center for Disease Control and Prevention, Korean women (n=10,710) had the lowest prevalence of GDM (2.9%) compared to other United States Asian subgroups including Japanese (5.7%) and Chinese (5.4%) [7]. There is probably some re-

Corresponding author: Catherine Kim
Departments of Medicine, Obstetrics and Gynecology, University of Michigan Medical School, Room 430W, 2800 Plymouth Rd Building 16, Ann Arbor, MI 48109, USA
E-mail: cathkim@umich.edu

gional variation, as ethnic Korean women in the United States have been noted to have a slightly higher GDM prevalence (4.7%) in medical center-based reports [8].

BMI and gestational weight gain

In several meta-analyses of primarily non-Asian populations, prepregnancy BMI has been the most significant risk factor for GDM [9,10]. In one report of 70 studies [10], women with BMIs <20 kg/m^2 had decreased odds of GDM compared to women with BMIs 20 to 24.9 kg/m^2; women who had BMIs 25 to 29.9 kg/m^2 had roughly a 2-fold increased odds of diabetes; women who were moderately obese (BMI 30 to 34.9 kg/m^2) had a 3-fold increased odds; and women who were morbidly obese (BMIs ≥35 kg/m^2) had a 5-fold increased odds [10]. In the United States, the population-attributable fraction of GDM for prepregnancy obesity, or the proportion of cases of GDM that would be averted if obesity were corrected, has been estimated at 46% [11].

Among Korean women, prepregnancy BMI is a risk factor for GDM [6]. However, fewer Korean women with GDM are overweight or obese, even using lower Asian-specific cutpoints for obesity. In one hospital-based report, a prepregnancy BMI >25 kg/m^2 was associated with increased odds of GDM compared to a BMI 18 to 22.9 kg/m^2 (odds ratio [OR], 4.46; 95% confidence interval [CI], 2.63 to 7.59), while greater gestational weight gain was not associated with increased risk of GDM. This report also suggested that the obesity epidemic has not reached the proportion of the United States and other European countries. In this cohort, which consisted of deliveries between 2007 and 2009, only 9.8% of the 2,413 gravidas were overweight (BMI 23 to 24.9 kg/m^2 for guidelines specific to Asians) and only 8.5% of gravidas had BMIs >25 kg/m^2 [6]. Therefore, the population attributable fraction of GDM due to obesity is low among Koreans.

Among non-Koreans, gestational weight gain may increase risk of GDM beyond prepregnancy BMI. In one study, women who gained 0.41 kg/week or more had increased risk of GDM (OR, 1.74; 95% CI, 1.16 to 2.60) compared to women in the lowest tertile of weight gain (<0.27 kg/wk) after adjustment for other GDM risk factors including age and prepregnancy BMI [12]. Increased gestational weight gain through 24 weeks combined with elevated prepregnancy BMI appears to confer particular risk; in one series, women with GDM had higher prepregnancy BMI and greater gestational weight gain compared to controls [13]. However, the risk of GDM was similar in women who had low or normal prepregnancy BMIs and high levels of gestational weight gain, compared to women who had low or normal prepregnancy BMIs and lower levels of gestational weight gain [13].

In contrast, among Koreans, one study found no linear association between gestational weight gain and GDM risk apart from prepregnancy BMI [6]. It is possible that this is because Korean women who were underweight or normal weight prior to pregnancy had the greatest gestational weight gain, 13.4 kg (SD 4.2 kg), and the majority of women were within Institute of Medicine guidelines for gestational weight gain [6]. Park et al. [14] also noted that overweight women had increased odds of GDM, but tended to have lesser gestational weight gain throughout the pregnancy, possibly because of intentional lifestyle changes; of note, it is unclear whether gestational weight gain before the GDM diagnosis, typically at 24 weeks gestation, was associated with GDM risk.

Heritability

Family history of diabetes increases risk for GDM in both non-Korean and Korean populations. In non-Korean populations, women with a maternal history of diabetes (OR, 3.0; 95% CI, 1.2 to 7.3), paternal history (OR, 3.3; 95% CI, 1.1 to 10.2), or sibling history (OR, 7.1; 95% CI, 1.6 to 30.9) had greater risk of GDM than women without a family history [15]. Similarly, among Korean women, the risk of developing GDM doubled with a parental history and increased 5-fold in cases with a sibling history [16]. In both Korean and non-Korean populations, a sibling with a family history of diabetes conferred greater risk than a parent with such a history, and having any family history of diabetes increased risk of GDM compared to no history. These studies suggest the importance of shared environmental exposures and genetic susceptibility.

Since GDM and type 2 diabetes both involve defects in insulin secretion in response to insulin resistance, investigators have examined whether genetic variants conferring increased risk for type 2 diabetes also increase risk for GDM. Among non-Korean populations, and specifically Danish women, type 2 diabetes risk variants also conferred increased risk for GDM [17]. The presence of a greater number of high-risk alleles conferred greater risk, and the magnitude of GDM risk conferred by these alleles was similar to that observed for diabetes risk [17]. Variants were associated with impaired β-cell function, insulin resistance, and obesity. Variants for transcription factor 7-like 2 and glucokinase increase risk for elevated fasting

glucose during pregnancy, probably through insulin secretion, and consequently, the latter has also been associated with macrosomia in Europeans [18].

Among Korean women, variants for cyclin-dependent kinase 5 (CDK5) regulatory subunit-associated protein 1-like 1 and melatonin receptor 1B (MTNR1B) were associated with increased risk for GDM [19]. CDKAL1 has been postulated to affect β-cell compensation [20]. MTNR1B, a G-protein-coupled receptor, is also present in β-cells and therefore may affect insulin secretion [21]. Unlike the studies in non-Koreans, loci associated with insulin resistance and obesity were not associated with GDM, underlining the role of impaired insulin secretion in GDM pathophysiology. The Korean cohort was smaller, and the power to detect associations with particular variants may have been limited, or it is possible that these variants have a lesser impact in Koreans compared to non-Koreans.

While at least 41 genetic loci increase risk for type 2 diabetes or abnormalities of carbohydrate metabolism, these known loci explain a small proportion of the heritability of type 2 diabetes [22]. Similarly, maternal genetic risk did not improve discriminatory ability for predicting fetal anthropometrics, and known genotypes reflect less than 1% of variance in maternal glucose levels [18]. However, presence of specific polymorphisms can be used in conjunction with clinical characteristics to predict when women with histories of GDM convert to type 2 diabetes. Kwak et al. [23] found that women with histories of GDM who had specific variants for CDK inhibitors (CDKNA/2B) and hematopoietically expressed homeobox, associated with impaired β-cell replication and secretion, respectively, had a greater risk for type 2 diabetes within 2 months after delivery than women who had variants in CDKAL1.

Intrauterine deprivation

The Barker hypothesis, formulated by David Barker, posits that intrauterine deprivation is a risk factor for adult chronic disease including diabetes [24]. Several reports in non-Korean populations suggest that markers of intrauterine deprivation, including low birthweight, may increase risk for gestational diabetes [25,26]. Mechanisms may include fewer β-cells among small for gestational age infants [27] or fetal insulin resistance leading to lesser growth *in utero* [28]. Therefore, impaired fetal growth combined with rapid weight gain in childhood may particularly stress the β-cell. Exposure to excess glucocorticoids may also play a role, as babies small for gestational age have higher glucocorticoid levels than babies who are larger [29].

To our knowledge, there have not been reports examining the association between birth weight and risk of GDM in Koreans. However, there are several reports examining other markers of intrauterine and early childhood development. Height is another marker for intrauterine deprivation, in that babies who are small for gestational age tend to be significantly shorter than babies who are larger for gestational age [30]. Among Polish mothers, women with GDM have been slightly but significantly shorter than women without GDM (165.7 cm vs. 163.8 cm; $P<0.001$), an association that persisted even after adjustment for other measures such as age and prepregnancy BMI [31]. Similarly, among Koreans, women with GDM are slightly but significantly shorter than women with normal glucose tolerance (158 cm vs. 160 cm; $P<0.001$) [32].

PERINATAL OUTCOMES

Among non-Korean populations, women with GDM are at greater risk for perinatal complications than women without GDM [33]. Maternal complications include preeclampsia and primary cesarean section, and neonatal complications include greater infant birth weight, large for gestational age infants, and necessity of phototherapy for hyperbilirubinemia. Complications have the strongest associations with the 1-hour glucose value on the index oral glucose tolerance test (OGTT) [33]. Similarly, prevalence of these complications was highest among Korean women with GDM compared to women with no elevated glucose levels on the index OGTT (39.2% vs. 22.3%) [34,35]. Risk of a large for gestational age infant is related to degree of elevation of all of the glucose values, in that the odds of a large for gestational age infant doubled with each 100 unit increase in area under the curve on the index OGTT [36]. However, in both non-Korean [37] and Korean women [38], even the elevation of only the 1-hour value on the OGTT, in the absence of a diagnosis of GDM, increases risk of complications.

Alterations in other metabolic parameters besides glucose are associated with macrosomia, underlining the fact that protein and lipid abnormalities accompany glucose intolerance. Among non-Korean women with GDM, maternal free fatty acid levels and triglyceride levels at delivery correlate with neonatal weight and fat mass, suggesting that maternal lipid profiles influence neonatal weight [39]. The investigators speculated that women with GDM had enhanced placental transport or enhanced lipolysis because of fetal insulin resistance

[40]. Among Korean women with GDM, maternal fasting triglyceride levels at 24 to 32 weeks gestation was also associated with increased risk of large for gestational age infants, even after adjustment for other risk factors such as elevated prepregnancy BMI and gestational weight gain [41].

Maternal prepregnancy BMI is a risk factor for macrosomia among non-Korean populations with GDM. In the Hyperglycaemia and Adverse Pregnancy Outcome Study, maternal BMI at the time of the index OGTT and hyperglycemia confer independent risks for macrosomia [42]. Others have reported that the effects of GDM and maternal prepregnancy BMI may vary by race/ethnicity, in that GDM conferred greater risk for macrosomia among non-Hispanic blacks than whites [43]. Among Korean women with GDM, the relationship between maternal prepregnancy BMI and macrosomia is not as strong as in non-Korean women. In one series, Korean women with GDM had a BMI of 22.9 kg/m^2 (SD 3.5 kg) compared to controls who had a BMI of 22.0 kg/m^2 (SD 2.8 kg) [35]. The infants of women with GDM still had excessive fetal growth and hyperinsulinemia as indicated by cord C-peptide and insulin concentrations [35].

Limiting gestational weight gain among Korean women with GDM may lower the risk of macrosomia; however, the parameters of gestational weight gain may need to be quite low [44]. In one Korean report, low gestational weight gain in was defined according to Institute of Medicine standards as less than 11.5, 6.8, and 5.0 kg for women who were normal weight, overweight, or obese before pregnancy [44] and averaged only 2.4 kg for overweight and obese women. Women with GDM who had low levels of gestational weight gain had macrosomia less often than women with excessive gestational weight gain, despite similar fasting glucose levels [44]. While gestational weight gain was not associated with any adverse outcomes, including small for gestational age infants, these results suggest that limits on gestational weight gain for minimization of macrosomia may differ between Korean and non-Asian women, and may need to be lower than is recommended by current guidelines.

POSTPARTUM MATERNAL OUTCOMES

It is well-established that women with GDM are at risk for glucose intolerance after delivery. Theoretically, several variables could influence postpartum maternal glucose tolerance: maternal insulin sensitivity and secretion prior to pregnancy, intrapartum stresses upon β-cell function, intrapartum accretion of energy stores that persist after delivery, and postpartum behaviors. As it is unknown whether pregnancy accelerates declines in β-cell reserve, the relative importance of intrapartum and postpartum factors is not clear: parity, apart from weight gain, has inconsistent associations with postpartum diabetes [45-48]. In addition, there are no studies that include precise measures of β-cell function, such as hyperinsulinemic euglycemic glucose clamp studies, that compare insulin disposition before and after high-risk pregnancies. However, cross-sectional data suggest that gestational weight gain is less important than prepregnancy factors among Korean women, because both women with GDM (n=269) and without GDM (n=306) gained approximately 7.5 kg during pregnancy (P=0.94) [49] but differed significantly in prepregnancy BMI.

Among non-Korean populations, the risk of GDM recurrence in one report (n=65,132) [50] was 41%, compared to 4% among women without GDM in their first pregnancy. Korean women with histories of GDM are also at increased risk for recurrence of GDM [51]. Kwak et al. [51] found that among women who had another pregnancy, 45% had recurrent GDM, a strikingly similar estimate to non-Koreans. Non-Koreans with GDM are at increased risk of postpartum diabetes as well: a 2007 meta-analysis reported that women with histories of GDM had a higher risk for diabetes than women without such histories (relative risk [RR], 7.43; 95% CI, 4.79 to 11.51) [52]. Korean women with histories of GDM are also at increased risk for postpartum diabetes [53-55]. Compared to Korean women without histories of GDM, Korean women with GDM had a 3.7 increased odds (OR, 3.7; 95% CI, 2.2 to 6.3) for developing diabetes over approximately 2 years [54], after adjustment for potential confounders such as age, family history of diabetes, education, income, smoking alcohol use, waist circumference, blood pressure, and lipid levels. Over 5 years, approximately 41% of Korean women with GDM developed type 2 diabetes [53].

BMI and weight as risk factors for postpartum glucose tolerance

Postpartum weight is strongly associated with increased risk of recurrent GDM as well as diabetes. In a systematic review conducted in 2009, body fat measures had the most consistent associations with diabetes risk compared to other types of factors including age, parity, and family history of diabetes [56]. Specifically, prepregnancy BMI was associated with significantly

increased risk of future diabetes after a GDM delivery; for every 1 kg increase in prepregnancy weight, there was a 40% increase in odds of developing type 2 diabetes (OR, 1.40; 95% CI, 1.20 to 1.60). Intrapartum weight measures and postpartum weight measures were also associated with increased diabetes risk [56]. Peters et al. [45] reported that for every 4.5 kg increase in weight postpartum, there was a 2-fold increase in the risk of type 2 diabetes, even after adjustment for other factors including postpartum BMI, OGTT results, and breastfeeding. While this finding was not consistent across all older reports [57], more recent reports suggest that maternal weight gain in the United States between pregnancies might play a larger role in postpartum glucose intolerance, perhaps due to the aforementioned steady increase in BMI over the past decade among women of reproductive age [2]. In one recent examination of 22,351 women in a multiethnic population in northern California, women had a significant increase in their odds of GDM in their subsequent pregnancy with each unit of BMI gained between pregnancies [58]. A higher absolute level of BMI before the subsequent pregnancy also increased risk of GDM in that subsequent pregnancy [58].

Among Korean women, absolute levels of BMI between pregnancies and weight between pregnancies predict GDM in the subsequent pregnancies [51]. In particular, visceral fat levels are associated with future risk of glucose intolerance; Cho et al. [53] compared the strength of association between postpartum BMI, weight, skin thickness, waist-hip ratio and waist circumference, and diabetes risk. Waist circumference as characterized by quartiles and body fat measures had the strongest associations, suggesting that adipose tissue as opposed to other tissue compartments and visceral fat deposition as opposed other types of fat deposition conferred the highest risk for diabetes. Korean women with GDM at one year postpartum have greater proportion of visceral fat than Korean women without histories of GDM, and as in previous studies of Korean women with GDM, women were not obese; average BMI was 21.8 kg/m^2 (SD 2.4 kg) in controls versus 22.5 kg/m^2 (SD 2.8 kg) in women with GDM with postpartum normal glucose tolerance [59]. Insulin sensitivity, as measured by intravenous glucose tolerance tests, was associated with visceral fat even after adjustment for body weight and BMI [59].

However, among Koreans, weight gained between pregnancies has not been associated with GDM risk [51]. It is unclear why intrapartum weight gain was not associated with risk of recurrent GDM in Korean women but has been in the United States. One possible explanation is that Korean gain relatively smaller amounts of weight between pregnancies; intrapartum weight gain was fairly small among Korean women, 1.2 kg (3.7) [51], whereas the majority of United States women gained over 2.25 kg [58]. Therefore, weight gain between pregnancies was larger and more likely to increase demand on the β-cell in the next pregnancy among United States women. Another, possibly concurrent explanation is suggested by the fact that in the United States report, women who were not overweight at their index GDM pregnancy but who lost weight after their index pregnancy did not significantly reduce their odds of future GDM [58]. While it is not known whether these women were more likely to be Asian, it is possible that weight is not as strong a risk factor for impaired insulin secretion or insulin sensitivity in a subset of women with GDM.

One explanation for the increased risk of GDM observed at lower cutpoints for BMI among Koreans could be a higher proportion of visceral fat compared to overall BMI among Koreans [60]. While Korean and other east Asian women have not been compared directly to other racial/ethnic groups, Korean women may have relatively greater proportions of visceral fat for specific levels of BMI compared to non-Hispanic whites; such racial/ethnic differences in proportions of visceral fat to body weight have been observed between other race/ethnicities [61]. Korean premenopausal women specifically have lower correlations between visceral fat and anthropometric measurements such as waist circumference compared to Korean postmenopausal women or men [62].

Metabolic markers

Adipose tissue is now recognized as an endocrine organ as well as a lipid storage compartment. The adipokines, or adipose-derived hormones, have been linked with risk of postpartum glucose intolerance particularly in women with histories of GDM. Among non-Koreans, women with histories of GDM have lower adiponectin independent of obesity and insulin sensitivity than women without such histories [63]. Low adiponectin levels during pregnancy are associated with degree of glycemia postpartum [64]. Among non-Koreans, lower adiponectin levels prepregnancy have been linked to increased risk for GDM, suggesting that to some extent these abnormalities precede the GDM pregnancy. Hedderson et al. [65] have reported that women in the lowest quartile of adiponectin have a 5-fold increased risk of GDM (OR, 5.2; 95% CI, 2.6 to 10.1) compared to women in the lowest quartile. The association

between lower adiponectin and higher glucose levels is also present in the first and early second trimester of pregnancy [66,67] and later in pregnancy [68], independent of BMI.

Similarly, Korean women with histories of GDM and postpartum diabetes had higher retinol binding protein 4 (RBP4) and lower adiponectin than women with histories of GDM and normal glucose tolerance, while women with impaired glucose tolerance had intermediate levels [69]. Leptin and resistin did not differ by GDM status [69]. Although RBP4 and adiponectin are synthesized by adipose tissue, there was no correlation between RBP4 or adiponectin concentrations with visceral fat.

Insulin use during the index pregnancy

The degree of β-cell impairment during the index pregnancy is reflected by decreased insulin levels as well as insulin use, as opposed to dietary or other pharmacotherapies. Thus, insulin use and endogenous levels during the index pregnancy reflect postpartum risk of glucose intolerance. Particularly in populations at high-risk for type 1 diabetes such as northern Europeans, insulin use may reflect autoantibody mediated β-cell impairment rather than from demand imposed by insulin resistance. In a cohort of 437 German women with GDM, 148 required insulin and of these women, 30.4% were autoantibody positive for islet cell antibodies, insulin autoantibodies, or glutamic acid decarboxylase (GAD) antibodies [48]. Among these women, 30% developed type 1 diabetes by 2 years postpartum, compared with 2% of antibody negative patients [48].

Among Korean women, lower insulin levels (both fasting and postchallenge) during the index pregnancy were associated with increased risk of recurrent GDM [51]. In a 2009 systematic review of 14 articles which included one report in Koreans, insulin use and anthropometric measures were most strongly associated with increased risk of GDM recurrence [56]. As in northern Europeans, need for insulin may reflect impending type 1 diabetes, rather than insulin resistance due to visceral fat or adiposity. Among 887 Korean with GDM, only 1.7% (n=15) had antibodies to GAD, but of these women, approximately half (n=7) required insulin therapy during the index pregnancy as opposed to 23% of Korean women with GDM who were GAD antibody negative [70]. While only 12 of the GAD antibody positive women were examined postpartum, 33% developed diabetes postpartum compared to a 7% incidence of diabetes among GAD antibody negative women [70].

Along with insulin levels and insulin use, glucose levels during and after the index pregnancy will reflect maternal insulin sensitivity and secretion and thus risk for postpartum glucose intolerance. In a 2009 review of 11 articles in primarily non-Korean populations [71], elevations in prenatal OGTT values fasting were all associated with increased diabetes risk, with the strongest associations observed with fasting glucose and 1-hour glucose [37,72-81]. Women with a greater number of abnormal values elevated fasting or postchallenge values had greater risk [82]. Among Korean women, impaired glucose tolerance after the index pregnancy was associated with increased risk of GDM recurrence compared to normal glucose levels after the index pregnancy (RR, 2.31; 95% CI, 1.24 to 4.30) [51].

Cardiovascular dysfunction

Among other racial/ethnic groups, GDM is associated with increased risk of cardiovascular dysfunction, although it is unclear whether this occurs apart from a diagnosis of postpartum glucose-intolerance and diabetes. Specifically, among non-Koreans, women with histories of GDM had greater vascular resistance, lower stroke volume, lower cardiac output [83]. Small cross-sectional studies conflict as to whether flow mediated dilation is impaired among women with histories of GDM [84]. Among Italian women, women with GDM had higher carotid intimal medial thickness at approximately 6.5 years postpartum compared to women without histories of GDM [85], even after adjustment for other cardiovascular disease (CVD) risk factors. Other have noted that GDM is associated with increased risk of cardiovascular events and hospitalizations for CVD, although the association between GDM and cardiovascular event risk was attenuated by adjusting for diabetes [86,87].

Among Koreans, carotid intimal medial thickness has not been reported to differ at 1 year postpartum between women with and without GDM [88], unlike the Italian study mentioned in the preceding paragraph. While explanations for the differences between non-Korean and Korean populations are speculative, the lack of relationship at 1 year postpartum in the Korean women could be attributed to the earlier examination and younger ages of the Korean women compared to the Italian women, or possibly less aggressive CVD among Korean with histories of GDM. To my knowledge, CVD events and other subclinical markers of atherosclerosis have not been examined in Korean women by GDM status.

BEHAVIORS AND BEHAVIORAL INTERVENTION

Among non-Korean populations with GDM, which tend to have a high prevalence of obesity, decreasing postpartum obesity can decrease diabetes risk. This was demonstrated in the Diabetes Prevention Program (DPP), a randomized controlled trial of lifestyle change versus metformin versus placebo, which had inclusion criteria of overweight and glucose intolerance [88]. Among the 350 women with histories of GDM, randomization to intensive lifestyle change targeting weight reduction led to significant reductions in diabetes incidence compared to placebo; metformin had similar benefit [89]. It is worth noting that DPP women may differ from the typical postpartum GDM population, in that women with GDM in the DPP were approximately 43±8 years of age, and about 12 years from their last delivery; it was not known whether this was their GDM delivery. Thus, infants or young children presumably had matured and presented less of a barrier to lifestyle modification, and GDM women who were at extremely high risk for diabetes may have converted soon after delivery. Moreover, the mean weight loss at 3 years was only 1.6 kg among with GDM after 3 years, compared to 4.0 kg among women without GDM.

Among non-Korean populations, lifestyle interventions closer to delivery have not yet proven to be effective. In another randomized controlled trial of 450 Chinese women with histories of GDM, there were no differences in glucose levels between the lifestyle intervention and control group at 3 years [90]. In another randomized trial in the United States [91], randomization of postpartum GDM women to lifestyle change (n=100) versus control (n=100) did not result in increased weight loss, although between arm differences in these outcomes were close to meeting statistical significance (P<0.10 but P>0.05); a larger trial is currently underway.

It is not clear whether weight loss interventions similar to the DPP would improve glucose tolerance among Korean women with histories of GDM, for several reasons. Although BMI is a risk factor for diabetes, the relatively low prevalence of overweight and obesity compared to non-Korean populations, even using lower cutpoints for Asians, raises the possibility that interventions targeting body mass might have a relatively reduced impact. Similarly, randomized trials in the United States are underway to limit gestational weight gain, but the relatively small amounts of gestational weight gain among Koreans combined with the lack of association between gestational weight gain and postpartum risk suggest that such interventions might have less of an impact in Koreans.

It is possible that other types of lifestyle changes other than those strictly targeting weight loss might decrease diabetes risk in Koreans. Among non-Koreans [92] and Koreans [87,93] with histories of GDM, unhealthy diets, indicated by greater fat intake as a proportion of caloric intake, are associated with diabetes. Among non-Koreans, the risk reduction was partially mediated by body mass changes [92]. Among Korean women with histories of GDM, women with postpartum diabetes had greater animal fat intake compared to women who did not [87]. While breastfeeding has been found to beneficial in non-Korean populations with histories of GDM for reduction of diabetes risk [94], apart from changes in weight gain, the impact of breastfeeding upon glucose tolerance has been less striking among Koreans [93].

Insulin sensitizers such as thiazolidinediones have been shown to reduce diabetes risk among United States Mexican women [95]. However, their current use is limited by concerns of increased risk to the heart, liver, bones, and bladder, as well as questions about safety in future pregnancies and general reluctance to prescribe lifetime medications for prevention in a reproductive-aged population. Theoretically, based upon the DPP results, metformin would reduce diabetes risk among overweight women with GDM and glucose intolerance, but it is not known whether this benefit would be observed in non-obese women with glucose intolerance, or among populations with normal postpartum glucose levels.

CONCLUSIONS

An increasing proportion of pregnancies worldwide are affected by glucose intolerance, in contrast to the relative infrequency of GDM among Korean women. These differences may be attributed to both genetic and environmental factors, particularly the lower proportion of obesity in Korean women. Population-based measures aimed at obesity and interventions targeting postpartum weight gain have proven difficult to translate in the immediate postpartum years among non-Korean populations. It is unknown whether such interventions would address the prenatal or postpartum risk in Korean women with GDM. However, GDM risk and postpartum risk among Korean GDM women may have different relationships with obesity than in non-Koreans, suggesting that additional strategies for addressing β-cell impairment need to be explored. Population-

based data on anthropometrics, dietary habits, and physical activity as well as glucose tolerance in Korean women could yield suggestions for GDM prevention and treatment in non-Koreans.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

Dr. Kim was supported by R01 064557 from the National Institutes of Health.

REFERENCES

1. Xiang AH, Kjos SL, Takayanagi M, Trigo E, Buchanan TA. Detailed physiological characterization of the development of type 2 diabetes in Hispanic women with prior gestational diabetes mellitus. Diabetes 2010;59:2625-30.
2. Rasmussen KM, Yaktine AL, Institute of Medicine (U.S.) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight gain during pregnancy: reexamining the guidelines. Washington, DC: National Academies Press; 2009.
3. Ferrara A, Kahn HS, Quesenberry CP, Riley C, Hedderson MM. An increase in the incidence of gestational diabetes mellitus: Northern California, 1991-2000. Obstet Gynecol 2004; 103:526-33.
4. Dabelea D, Snell-Bergeon JK, Hartsfield CL, Bischoff KJ, Hamman RF, McDuffie RS; Kaiser Permanente of Colorado GDM Screening Program. 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.
5. Jang HC, Cho NH, Jung KB, Oh KS, Dooley SL, Metzger BE. Screening for gestational diabetes mellitus in Korea. Int J Gynaecol Obstet 1995;51:115-22.
6. Choi SK, Park IY, Shin JC. The effects of pre-pregnancy body mass index and gestational weight gain on perinatal outcomes in Korean women: a retrospective cohort study. Reprod Biol Endocrinol 2011;9:6.
7. Rao AK, Cheng YW, Caughey AB. Perinatal complications among different Asian-American subgroups. Am J Obstet Gynecol 2006;194:e39-41.
8. Rao AK, Daniels K, El-Sayed YY, Moshesh MK, Caughey AB. Perinatal outcomes among Asian American and Pacific Islander women. Am J Obstet Gynecol 2006;195:834-8.
9. Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, Dietz PM. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care 2007;30:2070-6.
10. Torloni MR, Betran AP, Horta BL, Nakamura MU, Atallah AN, Moron AF, Valente O. Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis. Obes Rev 2009;10:194-203.
11. Kim SY, England L, Wilson HG, Bish C, Satten GA, Dietz P. Percentage of gestational diabetes mellitus attributable to overweight and obesity. Am J Public Health 2010;100:1047-52.
12. Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. Obstet Gynecol 2010;115:597-604.
13. Gibson KS, Waters TP, Catalano PM. Maternal weight gain in women who develop gestational diabetes mellitus. Obstet Gynecol 2012;119:560-5.
14. Park JH, Lee BE, Park HS, Ha EH, Lee SW, Kim YJ. Association between pre-pregnancy body mass index and socioeconomic status and impact on pregnancy outcomes in Korea. J Obstet Gynaecol Res 2011;37:138-45.
15. Kim C, Liu T, Valdez R, Beckles GL. Does frank diabetes in first-degree relatives of a pregnant woman affect the likelihood of her developing gestational diabetes mellitus or nongestational diabetes? Am J Obstet Gynecol 2009;201:576.
16. Rhee SY, Kim JY, Woo JT, Kim YS, Kim SH. Familial clustering of type 2 diabetes in Korean women with gestational diabetes mellitus. Korean J Intern Med 2010;25:269-72.
17. Lauenborg J, Grarup N, Damm P, Borch-Johnsen K, Jorgensen T, Pedersen O, Hansen T. Common type 2 diabetes risk gene variants associate with gestational diabetes. J Clin Endocrinol Metab 2009;94:145-50.
18. Freathy RM, Hayes MG, Urbanek M, Lowe LP, Lee H, Ackerman C, Frayling TM, Cox NJ, Dunger DB, Dyer AR, Hattersley AT, Metzger BE, Lowe WL Jr; HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: common genetic variants in GCK and TCF7L2 are associated with fasting and postchallenge glucose levels in pregnancy and with the new consensus definition of gestational diabetes mellitus from the International Association of Diabetes and Pregnancy Study Groups. Diabetes 2010; 59:2682-9.
19. Kwak SH, Kim SH, Cho YM, Go MJ, Cho YS, Choi SH, Moon

MK, Jung HS, Shin HD, Kang HM, Cho NH, Lee IK, Kim SY, Han BG, Jang HC, Park KS. A genome-wide association study of gestational diabetes mellitus in Korean women. Diabetes 2012;61:531-41.
20. Daval M, Gurlo T, Costes S, Huang CJ, Butler PC. Cyclin-dependent kinase 5 promotes pancreatic β-cell survival via Fak-Akt signaling pathways. Diabetes 2011;60:1186-97.
21. Lyssenko V, Nagorny CL, Erdos MR, Wierup N, Jonsson A, Spegel P, Bugliani M, Saxena R, Fex M, Pulizzi N, Isomaa B, Tuomi T, Nilsson P, Kuusisto J, Tuomilehto J, Boehnke M, Altshuler D, Sundler F, Eriksson JG, Jackson AU, Laakso M, Marchetti P, Watanabe RM, Mulder H, Groop L. Common variant in MTNR1B associated with increased risk of type 2 diabetes and impaired early insulin secretion. Nat Genet 2009;41:82-8.
22. Manolio TA, Collins FS, Cox NJ, Goldstein DB, Hindorff LA, Hunter DJ, McCarthy MI, Ramos EM, Cardon LR, Chakravarti A, Cho JH, Guttmacher AE, Kong A, Kruglyak L, Mardis E, Rotimi CN, Slatkin M, Valle D, Whittemore AS, Boehnke M, Clark AG, Eichler EE, Gibson G, Haines JL, Mackay TF, McCarroll SA, Visscher PM. Finding the missing heritability of complex diseases. Nature 2009;461:747-53.
23. Kwak SH, Choi SH, Jung HS, Cho YM, Lim S, Cho NH, Kim SY, Park KS, Jang HC. Clinical and genetic risk factors for type 2 diabetes at early or late post partum after gestational diabetes mellitus. J Clin Endocrinol Metab 2013;98:E744-52.
24. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM. Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X): relation to reduced fetal growth. Diabetologia 1993;36:62-7.
25. Innes KE, Byers TE, Marshall JA, Baron A, Orleans M, Hamman RF. Association of a woman's own birth weight with subsequent risk for gestational diabetes. JAMA 2002;287:2534-41.
26. Egeland GM, Skjaerven R, Irgens LM. Birth characteristics of women who develop gestational diabetes: population based study. BMJ 2000;321:546-7.
27. Van Assche FA, De Prins F, Aerts L, Verjans M. The endocrine pancreas in small-for-dates infants. Br J Obstet Gynaecol 1977;84:751-3.
28. Hattersley AT, Tooke JE. The fetal insulin hypothesis: an alternative explanation of the association of low birthweight with diabetes and vascular disease. Lancet 1999;353:1789-92.
29. de Boo HA, Harding JE. The developmental origins of adult disease (Barker) hypothesis. Aust N Z J Obstet Gynaecol 2006;46:4-14.
30. Westwood M, Kramer MS, Munz D, Lovett JM, Watters GV. Growth and development of full-term nonasphyxiated small-for-gestational-age newborns: follow-up through adolescence. Pediatrics 1983;71:376-82.
31. Ogonowski J, Miazgowski T. Are short women at risk for gestational diabetes mellitus? Eur J Endocrinol 2010;162:491-7.
32. Jang HC, Min HK, Lee HK, Cho NH, Metzger BE. Short stature in Korean women: a contribution to the multifactorial predisposition to gestational diabetes mellitus. Diabetologia 1998;41:778-83.
33. Ferrara A, Weiss NS, Hedderson MM, Quesenberry CP Jr, Selby JV, Ergas IJ, Peng T, Escobar GJ, Pettitt DJ, Sacks DA. Pregnancy plasma glucose levels exceeding the American Diabetes Association thresholds, but below the National Diabetes Data Group thresholds for gestational diabetes mellitus, are related to the risk of neonatal macrosomia, hypoglycaemia and hyperbilirubinaemia. Diabetologia 2007;50:298-306.
34. Lee WJ, Ahn SH, Kim HS, Yang JI, Kim YS, Oh JH, Han KS, Oh KS. Clinical manifestations and perinatal outcomes of pregnancies complicated with gestational impaired glucose tolerance and gestational diabetes mellitus. Korean J Obstet Gynecol 2001;44:1033-9.
35. Jang HC, Cho NH, Min YK, Han IK, Jung KB, Metzger BE. Increased macrosomia and perinatal morbidity independent of maternal obesity and advanced age in Korean women with GDM. Diabetes Care 1997;20:1582-8.
36. Kim S, Min WK, Chun S, Lee W, Chung HJ, Lee PR, Kim A. Quantitative risk estimation for large for gestational age using the area under the 100-g oral glucose tolerance test curve. J Clin Lab Anal 2009;23:231-6.
37. Retnakaran R, Qi Y, Sermer M, Connelly PW, Zinman B, Hanley AJ. Isolated hyperglycemia at 1 hour on oral glucose tolerance test in pregnancy resembles gestational diabetes mellitus in predicting postpartum metabolic dysfunction. Diabetes Care 2008;31:1275-81.
38. Kim HS, Chang KH, Yang JI, Yang SC, Lee HJ, Ryu HS. Clinical outcomes of pregnancy with one elevated glucose tolerance test value. Int J Gynaecol Obstet 2002;78:131-8.
39. Schaefer-Graf UM, Graf K, Kulbacka I, Kjos SL, Dudenhausen J, Vetter K, Herrera E. Maternal lipids as strong determinants of fetal environment and growth in pregnancies with gestational diabetes mellitus. Diabetes Care 2008;31:1858-63.
40. Schaefer-Graf UM, Meitzner K, Ortega-Senovilla H, Graf K, Vetter K, Abou-Dakn M, Herrera E. Differences in the implications of maternal lipids on fetal metabolism and growth between gestational diabetes mellitus and control pregnancies.

Diabet Med 2011;28:1053-9.
41. Son GH, Kwon JY, Kim YH, Park YW. Maternal serum triglycerides as predictive factors for large-for-gestational age newborns in women with gestational diabetes mellitus. Acta Obstet Gynecol Scand 2010;89:700-4.
42. HAPO Study Cooperative Research Group. Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Study: associations with maternal body mass index. BJOG 2010;117:575-84.
43. Hunt KJ, Marlow NM, Gebregziabher M, Ellerbe CN, Mauldin J, Mayorga ME, Korte JE. Impact of maternal diabetes on birthweight is greater in non-Hispanic blacks than in non-Hispanic whites. Diabetologia 2012;55:971-80.
44. Park JE, Park S, Daily JW, Kim SH. Low gestational weight gain improves infant and maternal pregnancy outcomes in overweight and obese Korean women with gestational diabetes mellitus. Gynecol Endocrinol 2011;27:775-81.
45. 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.
46. Manson JE, Rimm EB, Colditz GA, Stampfer MJ, Willett WC, Arky RA, Rosner B, Hennekens CH, Speizer FE. Parity and incidence of non-insulin-dependent diabetes mellitus. Am J Med 1992;93:13-8.
47. Gunderson EP, Lewis CE, Tsai AL, Chiang V, Carnethon M, Quesenberry CP Jr, Sidney S. A 20-year prospective study of childbearing and incidence of diabetes in young women, controlling for glycemia before conception: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Diabetes 2007;56:2990-6.
48. Fuchtenbusch M, Ferber K, Standl E, Ziegler AG. Prediction of type 1 diabetes postpartum in patients with gestational diabetes mellitus by combined islet cell autoantibody screening: a prospective multicenter study. Diabetes 1997;46:1459-67.
49. Yang SJ, Kim TN, Baik SH, Kim TS, Lee KW, Nam M, Park YS, Woo JT, Kim YS, Kim SH. Insulin secretion and insulin resistance in Korean women with gestational diabetes mellitus and impaired glucose tolerance. Korean J Intern Med 2013;28:306-13.
50. Getahun D, Nath C, Ananth CV, Chavez MR, Smulian JC. Gestational diabetes in the United States: temporal trends 1989 through 2004. Am J Obstet Gynecol 2008;198:525.
51. Kwak SH, Kim HS, Choi SH, Lim S, Cho YM, Park KS, Jang HC, Kim MY, Cho NH, Metzger BE. Subsequent pregnancy after gestational diabetes mellitus: frequency and risk factors for recurrence in Korean women. Diabetes Care 2008;31:1867-71.
52. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773-9.
53. 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.
54. Lee H, Jang HC, Park HK, Metzger BE, Cho NH. Prevalence of type 2 diabetes among women with a previous history of gestational diabetes mellitus. Diabetes Res Clin Pract 2008;81:124-9.
55. Jang HC. Gestational diabetes in Korea: incidence and risk factors of diabetes in women with previous gestational diabetes. Diabetes Metab J 2011;35:1-7.
56. Baptiste-Roberts K, Barone BB, Gary TL, Golden SH, Wilson LM, Bass EB, Nicholson WK. Risk factors for type 2 diabetes among women with gestational diabetes: a systematic review. Am J Med 2009;122:207-14.
57. Kim C, Berger DK, Chamany S. Recurrence of gestational diabetes mellitus: a systematic review. Diabetes Care 2007;30:1314-9.
58. Ehrlich SF, Hedderson MM, Feng J, Davenport ER, Gunderson EP, Ferrara A. Change in body mass index between pregnancies and the risk of gestational diabetes in a second pregnancy. Obstet Gynecol 2011;117:1323-30.
59. Lim S, Choi SH, Park YJ, Park KS, Lee HK, Jang HC, Cho NH, Metzger BE. Visceral fatness and insulin sensitivity in women with a previous history of gestational diabetes mellitus. Diabetes Care 2007;30:348-53.
60. Neeland IJ, Turer AT, Ayers CR, Powell-Wiley TM, Vega GL, Farzaneh-Far R, Grundy SM, Khera A, McGuire DK, de Lemos JA. Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. JAMA 2012;308:1150-9.
61. Albu JB, Murphy L, Frager DH, Johnson JA, Pi-Sunyer FX. Visceral fat and race-dependent health risks in obese nondiabetic premenopausal women. Diabetes 1997;46:456-62.
62. Kim HI, Kim JT, Yu SH, Kwak SH, Jang HC, Park KS, Kim SY, Lee HK, Cho YM. Gender differences in diagnostic values of visceral fat area and waist circumference for predicting metabolic syndrome in Koreans. J Korean Med Sci 2011;26:906-13.
63. Winzer C, Wagner O, Festa A, Schneider B, Roden M, Bancher-Todesca D, Pacini G, Funahashi T, Kautzky-Willer A. Plasma adiponectin, insulin sensitivity, and subclinical inflammation in women with prior gestational diabetes mellitus. Diabetes Care 2004;27:1721-7.
64. Retnakaran R, Qi Y, Connelly PW, Sermer M, Hanley AJ, Zinman B. Low adiponectin concentration during pregnancy pre-

dicts postpartum insulin resistance, beta cell dysfunction and fasting glycaemia. Diabetologia 2010;53:268-76.
65. Hedderson MM, Darbinian J, Havel PJ, Quesenberry CP, Sridhar S, Ehrlich S, Ferrara A. Low prepregnancy adiponectin concentrations are associated with a marked increase in risk for development of gestational diabetes mellitus. Diabetes Care 2013;36:3930-7.
66. Lacroix M, Battista MC, Doyon M, Menard J, Ardilouze JL, Perron P, Hivert MF. Lower adiponectin levels at first trimester of pregnancy are associated with increased insulin resistance and higher risk of developing gestational diabetes mellitus. Diabetes Care 2013;36:1577-83.
67. Nicholson W, Wang NY, Baptiste-Roberts K, Chang YT, Powe NR. Association between adiponectin and tumor necrosis factor-alpha levels at eight to fourteen weeks gestation and maternal glucose tolerance: the Parity, Inflammation, and Diabetes Study. J Womens Health (Larchmt) 2013;22:259-66.
68. Park S, Kim MY, Baik SH, Woo JT, Kwon YJ, Daily JW, Park YM, Yang JH, Kim SH. Gestational diabetes is associated with high energy and saturated fat intakes and with low plasma visfatin and adiponectin levels independent of prepregnancy BMI. Eur J Clin Nutr 2013;67:196-201.
69. Choi SH, Kwak SH, Youn BS, Lim S, Park YJ, Lee H, Lee N, Cho YM, Lee HK, Kim YB, Park KS, Jang HC. High plasma retinol binding protein-4 and low plasma adiponectin concentrations are associated with severity of glucose intolerance in women with previous gestational diabetes mellitus. J Clin Endocrinol Metab 2008;93:3142-8.
70. Yu SH, Park S, Kim HS, Park SY, Yim CH, Han KO, Yoon HK, Jang HC, Chung HY, Kim SH. The prevalence of GAD antibodies in Korean women with gestational diabetes mellitus and their clinical characteristics during and after pregnancy. Diabetes Metab Res Rev 2009;25:329-34.
71. Golden SH, Bennett WL, Baptist-Roberts K, Wilson LM, Barone B, Gary TL, Bass E, Nicholson WK. Antepartum glucose tolerance test results as predictors of type 2 diabetes mellitus in women with a history of gestational diabetes mellitus: a systematic review. Gend Med 2009;6 Suppl 1:109-22.
72. Catalano PM, Vargo KM, Bernstein IM, Amini SB. Incidence and risk factors associated with abnormal postpartum glucose tolerance in women with gestational diabetes. Am J Obstet Gynecol 1991;165(4 Pt 1):914-9.
73. Cheung NW, Helmink D. Gestational diabetes: the significance of persistent fasting hyperglycemia for the subsequent development of diabetes mellitus. J Diabetes Complications 2006;20:21-5.
74. 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.
75. 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.
76. 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.
77. 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.
78. Retnakaran R, Zinman B, Connelly PW, Sermer M, Hanley AJ. Impaired glucose tolerance of pregnancy is a heterogeneous metabolic disorder as defined by the glycemic response to the oral glucose tolerance test. Diabetes Care 2006;29:57-62.
79. Buchanan TA, Xiang AH, Kjos SL, Trigo E, Lee WP, Peters RK. Antepartum predictors of the development of type 2 diabetes in Latino women 11-26 months after pregnancies complicated by gestational diabetes. Diabetes 1999;48:2430-6.
80. Jang HC, Yim CH, Han KO, Yoon HK, Han IK, Kim MY, Yang JH, Cho NH. Gestational diabetes mellitus in Korea: prevalence and prediction of glucose intolerance at early postpartum. Diabetes Res Clin Pract 2003;61:117-24.
81. 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.
82. Pallardo F, Herranz L, Garcia-Ingelmo T, Grande C, Martin-Vaquero P, Janez M, Gonzalez A. Early postpartum metabolic assessment in women with prior gestational diabetes. Diabetes Care 1999;22:1053-8.
83. Heitritter SM, Solomon CG, Mitchell GF, Skali-Ounis N, Seely EW. Subclinical inflammation and vascular dysfunction in women with previous gestational diabetes mellitus. J Clin Endocrinol Metab 2005;90:3983-8.
84. Brewster S, Zinman B, Retnakaran R, Floras JS. Cardiometabolic consequences of gestational dysglycemia. J Am Coll Cardiol 2013;62:677-84.
85. Bo S, Valpreda S, Menato G, Bardelli C, Botto C, Gambino R,

Rabbia C, Durazzo M, Cassader M, Massobrio M, Pagano G. Should we consider gestational diabetes a vascular risk factor? Atherosclerosis 2007;194:e72-9.
86. Shah BR, Retnakaran R, Booth GL. Increased risk of cardiovascular disease in young women following gestational diabetes mellitus. Diabetes Care 2008;31:1668-9.
87. Hwang YJ, Park BK, Park S, Kim SH. A comparative study of eating habits and food intake in women with gestational diabetes according to early postpartum glucose tolerance status. Diabetes Metab J 2011;35:354-63.
88. Ku YH, Choi SH, Lim S, Cho YM, Park YJ, Park KS, Kim SY, Jang HC. Carotid intimal-medial thickness is not increased in women with previous gestational diabetes mellitus. Diabetes Metab J 2011;35:497-503.
89. Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, Fowler S, Kahn SE; Diabetes Prevention Program Research Group. Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions. J Clin Endocrinol Metab 2008;93:4774-9.
90. Shek NW, Ngai CS, Lee CP, Chan JY, Lao TT. Lifestyle modifications in the development of diabetes mellitus and metabolic syndrome in Chinese women who had gestational diabetes mellitus: a randomized interventional trial. Arch Gynecol Obstet 2014;289:319-27.
91. Ferrara A, Hedderson MM, Albright CL, Ehrlich SF, Quesenberry CP Jr, Peng T, Feng J, Ching J, Crites Y. A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial. Diabetes Care 2011;34:1519-25.
92. Tobias DK, Hu FB, Chavarro J, Rosner B, Mozaffarian D, Zhang C. Healthful dietary patterns and type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Arch Intern Med 2012;172:1566-72.
93. Kim SH, Kim MY, Yang JH, Park SY, Yim CH, Han KO, Yoon HK, Park S. Nutritional risk factors of early development of postpartum prediabetes and diabetes in women with gestational diabetes mellitus. Nutrition 2011;27:782-8.
94. Ziegler AG, Wallner M, Kaiser I, Rossbauer M, Harsunen MH, Lachmann L, Maier J, Winkler C, Hummel S. Long-term protective effect of lactation on the development of type 2 diabetes in women with recent gestational diabetes mellitus. Diabetes 2012;61:3167-71.
95. Buchanan TA, Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, Ochoa C, Tan S, Berkowitz K, Hodis HN, Azen SP. 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.