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## Gestational hypertension and chronic hypertension on the risk of diabetes among gestational diabetes women

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## ABSTRACT

**Aims:** We aimed to examine the association of gestational hypertension and chronic hypertension at the inter-conception examination with type 2 diabetes risk among women with a history of gestational diabetes. **Methods:** We conducted a population-based study among 1261 women who had a history of gestational diabetes at 1–5 years after delivery in Tianjin, China. Logistic regression or Cox regression was used to assess the associations of gestational hypertension and chronic hypertension at the inter-conception examination with pre-diabetes and type 2 diabetes risks.

**Results:** Gestational diabetic women who had a history of gestational hypertension but did not use antihypertensive drugs during pregnancy had a 3.94-fold higher risk (95% CI: 1.94–8.02) of developing type 2 diabetes compared with those who were normotensive in index pregnancy. Compared with gestational diabetic women who had normal blood pressure at the inter-conception examination, hypertensive women at the inter-conception examination were 3.38 times (95% CI: 1.66–6.87) and 2.97 times (95% CI: 1.75–5.05) more likely to develop diabetes and prediabetes, respectively. The odds ratios of type 2 diabetes and prediabetes associated with each 5 mmHg increase in systolic blood pressure were 1.25 (95% CI: 1.03–1.51) and 1.20 (95% CI: 1.06–1.35). Each 5 mmHg increase in diastolic blood pressure contributed to a 1.49-fold higher risk (95% CI: 1.18–1.88) for type 2 diabetes and a 1.42-fold higher risk (95% CI: 1.22–1.65) for prediabetes.

**Conclusions:** For women with prior gestational diabetes, gestational hypertension and chronic hypertension at the inter-conception examination were risk factors for type 2 diabetes.

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### 1. Introduction

Hyperglycemia and diabetes are rising globally and become major public health problems worldwide and the mortality burden of diabetes has shifted from high-income to low-income and middle-income countries (Lopez, Bailey, Rupnow, & Annunziata, 2014). Studies on ethnic difference in type 2 diabetes showed that Asian Americans were more likely to have type 2 diabetes and had poorer levels of glycemic

control and medication adherence (Lopez et al., 2014) compared with their white counterparts. In 2013, about 382 million people were estimated to have diabetes globally, and of them about 98.4 million (25.8%) were living in China (Guariguata et al., 2014).

Gestational diabetes mellitus (GDM) is defined as glucose intolerance with onset or first recognition during pregnancy. Women with a history of GDM have a higher risk of developing type 2 diabetes during their lifetime (Bellamy, Casas, Hingorani, & Williams, 2009). Besides, diabetes is also associated with high body mass index (BMI) and increased blood pressure (Dotevall, Johansson, Wilhelmsen, & Rosengren, 2004); more than 50% of diabetic patients have hypertension (Lastra, Syed, Kurukulasuriya, Manrique, & Sowers, 2014). Women with GDM have also been found to have an increased risk of gestational hypertension (Bryson, Ioannou, Rulyak, &

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Critchlow, 2003). Gestational hypertension, as a type of hypertensive disorders of pregnancy, is transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy. (Vest & Cho, 2012). Several prospective studies have assessed the association between gestational hypertension and the risk of incident type 2 diabetes after delivery, but the results are inconsistent; some studies have reported a positive association (Callaway et al., 2007; Engeland et al., 2011; Feig et al., 2013; Lykke et al., 2009) while others found no association (Kurabayashi et al., 2013; Savitz, Danilack, Elston, & Lipkind, 2014). All these studies were carried out among the general population of women with pregnancy. Although both GDM and gestational hypertension might be associated with an increased risk of type 2 diabetes, no study has evaluated the putative association between gestational hypertension and type 2 diabetes risk among women with GDM. Therefore, the aim of the current study was to assess whether the findings of both gestational diabetes and gestational hypertension in the index pregnancy, or evidence of chronic hypertension at an inter-conception exam performed greater than 2 years from the index pregnancy is associated with increased prevalence of type 2 diabetes or prediabetes.

## 2. Material and methods

### 2.1. Study population

Tianjin is the fourth largest city of China. Since 1999, all pregnant women who live in six urban districts of Tianjin have participated in the screening project for GDM and the average screening rate was over 91% during 1999–2008 (Zhang et al., 2011). All pregnant women participated in a 1-h oral glucose tolerance test (OGTT) with 50-g glucose load at 26–30 gestational weeks. Women who had plasma glucose  $\geq 7.8$  mmol/L were invited to undergo a 2-h OGTT with a 75-g glucose load at the Tianjin Women's and Children's Health Center. GDM was defined based on World Health Organization's criteria (WHO Consultation, 1999). Women with a 75-g glucose 2-h OGTT result confirming either diabetes (fasting glucose  $\geq 7$  mmol/L or 2-h glucose  $\geq 11.1$  mmol/L) or impaired glucose tolerance (IGT) (2-h glucose  $\geq 7.8$  and  $< 11.1$  mmol/L) were regarded as having GDM (Zhang et al., 2011). A total of 128,125 pregnant women took part in the GDM screening project December 1998 to December 2009; of them 6247 were diagnosed with GDM (Hu et al., 2012).

All pregnant women diagnosed with GDM between 2005 and 2009 in six urban districts ( $n = 4644$ ) were eligible for the Tianjin Gestational Diabetes Mellitus Prevention Program. Since we had set up a good health care registration system for mothers (including pregnant women) and their children, we first mailed a letter to inform the mothers about the study aims, and invited eligible mothers to participate in the baseline survey from August 2009 to July 2011 (Hu et al., 2012). The inclusion and exclusion criteria were described in detail before (Hu et al., 2012). A total of 1263 (participation rate = 27%) women with GDM aged  $> 24$  years finished the baseline survey (the inter-conception examination). The present study included 1261 women after excluding women with chronic hypertension ( $n = 2$ ) at the index pregnancy. There were no differences at 26–30 weeks' gestation in age (28.9 vs. 28.7 years), fasting glucose (5.34 vs. 5.34 mmol/L), 2-h glucose (9.23 vs. 9.16 mmol/L), and the prevalence of IGT (90.9% vs. 91.8%) and diabetes (9.1% vs. 8.2%) between the women who responded and those who did not. The study was approved by the Human Subjects Committee of the Tianjin Women's and Children's Health Center. Informed consent was obtained from each participant in the baseline survey.

### 2.2. Measurements

At the postpartum baseline survey, all participants filled out a questionnaire about their sociodemographic (age, marital status,

education, income, and occupation); history of GDM; family history (diabetes, coronary heart disease, stroke, cancer, and hypertension); medical history and drug treatments (hypertension, gestational hypertension, diabetes, and hypercholesterolemia); pregnancy outcomes (pre-pregnancy weight, weight gain during pregnancy, and number of children); dietary habits (a self-administered food frequency questionnaire to measure the frequency and quantity of intake of 33 major food groups and beverages during the past year); alcohol intake; smoking habits; passive smoking; and physical activity (the frequency and duration of leisure time and sedentary activities) (Wang et al., 2014). The women also completed the 3-day 24-h food records using methods for dietary record collection taught by a dietitian. The performance of 3-day 24-h food records (Li et al., 2006), the food frequency questionnaire (Li et al., 2006), and the above-mentioned questionnaire assessing physical activity (Ma et al., 2008) were validated in the China National Nutrition and Health Survey in 2002. Women who reported gestational hypertension, preeclampsia, severe preeclampsia, or eclampsia diagnosed by physician after 20 weeks of gestation on the questionnaire were classified as having a history of gestational hypertension at baseline survey.

Body weight, height, and blood pressure were measured for all women at the postpartum baseline survey, using the standardized protocol by specially trained research doctors. Height (without shoes) was measured to the nearest 0.1 cm, and weight was rounded to the nearest 0.1 kg. BMI was calculated by dividing weight in kilograms by the square of height in meters. Blood pressure was measured from the right arm using a standard mercury sphygmomanometer after 5 min of rest with the subject in the sitting position. Blood pressure was measured twice, and the mean value of the two measurements was used for the analysis. Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg by using 2007 European Society of Hypertension (ESH)-European Society of Cardiology (ESC) Guidelines for the management of arterial hypertension (Mansia et al., 2007).

### 2.3. Definition of type 2 diabetes and pre-diabetes at baseline survey

Blood samples were collected from all participants after an overnight fast of at least 12 h. All participants were given a standard 2-h 75-g oral glucose tolerance test (OGTT). Plasma glucose was measured using an automatic analyzer (TBA-120FR; Toshiba, Japan). Diabetes classification methods were established according to the American Diabetes Association's criteria (American Diabetes Association, 2009): diabetes (fasting glucose  $\geq 7.0$  mmol/L and/or 2-h glucose  $\geq 11.1$  mmol/L), prediabetes (either impaired fasting glucose [fasting glucose  $\geq 5.6$  and  $< 7.0$  mmol/L] and/or IGT [2-h glucose  $\geq 7.8$  and  $< 11.1$  mmol/L]) and normal glucose (fasting glucose  $< 5.6$  mmol/L and 2-h glucose  $< 7.8$  mmol/L).

### 2.4. Statistical analyses

The effect of gestational hypertension and status of using antihypertensive drugs on the risks of type 2 diabetes and prediabetes were assessed through both logistic regression models and Cox regression models. Logistic regressions were performed to estimate the association between blood pressure at the inter-conception examination and the risks of type 2 diabetes and prediabetes. Blood pressure at the inter-conception examination was evaluated as both categorical and continuous variables. According to 2007 ESH-ESC Guidelines (Mansia et al., 2007), systolic blood pressure was categorized as  $< 120$ , 120–129, 130–139, and  $\geq 140$  mmHg, diastolic blood pressure was classified as  $< 80$ , 80–84, 85–89, and  $\geq 90$  mmHg, and joint systolic/diastolic blood pressure level was cut off at the same values. Both Logistic regression and Cox regression were performed in three multivariable-adjusted models. Model 1 only adjusted for baseline age. In model 2, adjusted variables included baseline age, education, family history of diabetes,

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