



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



Xiaojing Yuan ^{a,1}, Huikun Liu ^{b,1}, Leishen Wang ^b, Shuang Zhang ^b, Cuiping Zhang ^b, Junhong Leng ^b, Ling Dong ^b, Li Lv ^b, Fengjun Lv ^b, Huiguang Tian ^b, Lu Qi ^{c,d}, Jaakko Tuomilehto ^{e,f,g,h,i}, Gang Hu ^{a,*}

^a Pennington Biomedical Research Center, Baton Rouge, LA

^b Tianjin Women's and Children's Health Center, Tianjin, China

^c Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA

^d Department of Nutrition, Harvard School of Public Health, Boston, MA, USA

^e Department of Public Health, University of Helsinki, Helsinki, Finland

^f Centre for Vascular Prevention, Danube-University Krems, Krems, Austria

^g Diabetes Prevention Unit, National Institute for Health and Welfare, Helsinki, Finland

^h Diabetes Research Group, King Abdulaziz University, Jeddah, Saudi Arabia

ⁱ Dasman Diabetes Institute, Dasman, Kuwait

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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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* Corresponding author at: Chronic Disease Epidemiology Laboratory, Pennington Biomedical Research Center, 6400 Perkins Road, Baton Rouge, LA 70808. Tel.: +1 225 763 3053; fax: +1 225 763 3009.

E-mail address: gang.hu@pbrc.edu (G. Hu).

¹ X.Y. and H.L. contributed equally to this work.

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 ≥ 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 ≥ 7 mmol/L or 2-h glucose ≥ 11.1 mmol/L) or impaired glucose tolerance (IGT) (2-h glucose ≥ 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 ≥ 140 mmHg or diastolic blood pressure ≥ 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 ≥ 7.0 mmol/L and/or 2-h glucose ≥ 11.1 mmol/L), prediabetes (either impaired fasting glucose [fasting glucose ≥ 5.6 and < 7.0 mmol/L] and/or IGT [2-h glucose ≥ 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 ≥ 140 mmHg, diastolic blood pressure was classified as < 80 , 80–84, 85–89, and ≥ 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,

Table 1

Baseline characteristics of women with gestational diabetes mellitus by the outcome during follow-up.

	Normal glucose (n = 779)	Pre-diabetes (n = 401)	Diabetes (n = 81)	P-value
Age at baseline survey (years)	32.3 ± 3.5	32.5 ± 3.5	32.7 ± 3.8	0.56
Time postpartum at baseline survey (months)	27.0 ± 10.5	27.3 ± 10.2	31.6 ± 11.4	0.001
Body mass index (kg/m ²)				
Before pregnancy	22.4 ± 3.0	23.9 ± 3.4	25.6 ± 3.7	<0.001
At baseline survey	23.2 ± 3.4	25.4 ± 4.1	27.3 ± 4.0	<0.001
Blood pressure (mmHg)				
Systolic*	105 ± 10.5	110 ± 12.6	115 ± 15.1	<0.001
Diastolic†	72.0 ± 8.4	76.6 ± 10.4	80.7 ± 11.2	<0.001
Dietary intakes‡				
Energy consumption (kcal/day)	1685 ± 432	1715 ± 475	1708 ± 418	0.20
Fiber (g/day)	10.4 ± 4.1	10.5 ± 4.2	10.5 ± 4.5	0.82
Fat (% energy)	33.3 ± 6.3	33.8 ± 6.4	33.3 ± 6.4	0.45
Saturated fat (% energy)	8.0 ± 2.1	8.1 ± 2.0	7.9 ± 2.2	0.66
Monounsaturated fat (% energy)	13.5 ± 2.7	13.7 ± 2.8	13.7 ± 3.0	0.44
Polyunsaturated fat (% energy)	11.9 ± 2.9	12.1 ± 3.1	11.8 ± 2.9	0.60
Education (%)				
<13 years§	20.3	24.4	33.3	0.06
13–15 years	71.6	68.8	61.7	
≥16 years	8.1	6.7	4.9	
Family income (%)				
<5000 Yuan/month	25.2	29.4	40.7	0.01
5000–7999 Yuan/month	37.0	36.9	37.0	
≥8000 Yuan/month	37.9	33.7	22.2	
Family history of diabetes (%)	31.6	38.9	59.3	<0.001
Current smoking (%)	2.1	1.7	2.5	0.90
Passive smoking (%)	52.8	54.4	60.5	0.40
Current alcohol drinkers (%)	21.3	21.9	25.9	0.63
Leisure time physical activity (%)				
0 min/day	77.8	80.5	79.0	0.81
1–29 min/day	20.2	17.2	18.5	
≥30 min/day	2.1	2.2	2.5	
Sitting time at home (hours/day)	3.1 ± 2.1	3.3 ± 2.1	3.5 ± 2.3	0.13
History of gestational hypertension (%)				<0.001
No	94.9	92.5	76.5	
Yes and not using antihypertensive drugs	3.7	5.0	17.3	
Yes and using antihypertensive drugs	1.4	2.5	6.2	

Data are means ± standard deviation. One way ANOVA and chi-square tests were used to assess the difference between three groups.

* Systolic blood pressure median was 107.5 mmHg (interquartile range: 100–112.5 mmHg).

† Diastolic blood pressure median was 72.5 mmHg (interquartile range: 70–80 mmHg).

‡ Dietary intakes were measured by 3-d 24-h food records and FFQ.

§ Education years means number of years of school attendance.

|| 1 US dollar was 6.19 Chinese Yuan as of 02/02/2015.

smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, dietary fiber, total energy intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat. Model 3 was further adjusted for pre-pregnancy and baseline BMI on the basis of model 2. All statistical analyses were conducted with a significance level at 0.05 using IBM SPSS Statistics 21.0 (IBM SPSS, Chicago, IL).

3. Results

Characteristics of study participants are shown in [Table 1](#) and [Supplemental Table 1](#). Compared with GDM women with normal glucose, those who developed prediabetes and diabetes at the inter-conception examination had higher level of pre-pregnancy BMI, BMI and blood pressure at the inter-conception examination, longer follow-up time, lower education level and family income, and were more likely to have a history of gestational hypertension and a family history of diabetes.

[Table 2](#) presents results from three logistic regression models estimating the risk of type 2 diabetes among women with prior GDM. In total, 89 women had gestational hypertension during their index pregnancy and 94 women had chronic hypertension at the inter-conception exam. GDM women who had a history of gestational hypertension but did not use antihypertensive drugs had a 3.94-fold higher risk (95% CI: 1.94–8.02) of developing diabetes after delivery compared with those who were normotensive in index pregnancy.

Across all the three models, higher blood pressure at the inter-conception examination level was significantly associated with type 2 diabetes risk. GDM women who had systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg were more likely to have diabetes (OR: 3.38, 95% CI: 1.66–6.87) compared with those who had normal blood pressure (<120/80 mmHg). When considering systolic and diastolic blood pressure as continuous variables, the multivariable-adjusted ORs of diabetes were 1.25 (95% CI: 1.03–1.51) for each 5 mmHg increase in systolic blood pressure and 1.49 (95% CI: 1.18–1.88) for each 5 mmHg in diastolic blood pressure.

We also examined the impact of history of gestational hypertension and antihypertensive drugs use on the risks of prediabetes and diabetes using Cox regression models ([Supplemental Table 2](#)). Median value of follow-up after delivery was 2.05 (interquartile was 1.57 and 2.70). The observed results were very close to those of logistic regression models. Hazard ratio for type 2 diabetes among women who had a history of gestational hypertension but did not take antihypertensive drugs during pregnancy was 2.33 (95% CI: 1.26–4.29) compared with women who did not have gestational hypertension.

There was no difference in the risk of prediabetes among GDM women who had or did not have gestational hypertension ([Table 3](#)). Compared with GDM women with optimal blood pressure at the inter-conception examination (<120/80 mmHg), the ORs for having pre-diabetes were 1.56 (95% CI: 1.16–2.11) among GDM women who had normal blood pressure at the inter-conception examination (120–129/80–84 mmHg), and 2.97 (95% CI: 1.75–5.05) among GDM

Table 2
Odd ratios for type 2 diabetes by gestational hypertension and high blood pressure at the inter-conception examination.

	No. of participants	Odds ratios (95% confidence intervals)		
		Model 1*	Model 2†	Model 3‡
History of gestational hypertension				
No	1172	1.00	1.00	1.00
Yes and not using antihypertensive drugs	63	5.07 (2.65–9.69)	5.84 (2.96–11.5)	3.94 (1.94–8.02)
Yes and using antihypertensive drugs	26	4.23 (1.54–11.6)	3.37 (1.16–9.75)	2.09 (0.68–6.38)
Systolic blood pressure categories				
<120 mmHg	1029	1.00	1.00	1.00
120–129 mmHg	176	2.45 (1.42–4.23)	2.33 (1.32–4.10)	1.65 (0.91–3.00)
130–139 mmHg	32	4.39 (1.72–11.2)	3.94 (1.48–10.5)	2.31 (0.84–6.36)
≥140 mmHg	24	3.80 (1.25–11.6)	3.87 (1.20–12.5)	1.74 (0.49–6.16)
P for trend		<0.001	0.001	0.20
Systolic blood pressure as a continuous variable (5 mmHg increase)		1.50 (1.27–1.77)	1.47 (1.24–1.75)	1.25 (1.03–1.51)
Diastolic blood pressure categories (%)				
<80 mmHg	843	1.00	1.00	1.00
80–84 mmHg	282	2.21 (1.29–3.80)	2.26 (1.3–3.95)	1.66 (0.93–2.95)
85–89 mmHg	44	3.04 (1.13–8.21)	2.52 (0.90–7.05)	2.00 (0.70–5.73)
≥90 mmHg	92	5.75 (3.09–10.7)	5.94 (3.11–11.3)	3.35 (1.67–6.70)
P for trend		<0.001	<0.001	0.007
Diastolic blood pressure as a continuous variable (5 mmHg increase)		1.80 (1.46–2.22)	1.79 (1.44–2.23)	1.49 (1.18–1.88)
Systolic/diastolic blood pressure categories				
<120/80 mmHg	797	1.00	1.00	1.00
120–129/80–84 mmHg	322	2.26 (1.33–3.85)	2.31 (1.33–3.99)	1.70 (0.96–3.02)
130–139/85–89 mmHg	48	2.86 (1.06–7.74)	2.34 (0.83–6.56)	1.76 (0.61–5.07)
≥140/90 mmHg	94	5.82 (3.10–10.9)	6.11 (3.17–11.8)	3.38 (1.66–6.87)
P for trend		<0.001	<0.001	0.009

* Adjusted for age.

† Adjusted for age, education, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, dietary fiber, total energy intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat.

‡ Adjusted for variables in model 2 and also pre-pregnancy body mass index and baseline body mass index.

women who were hypertensive at the inter-conception examination (≥140/90 mmHg). When considering systolic and diastolic blood pressure as continuous variables, the multivariable-adjusted ORs of pre-diabetes associated with each 5 mmHg increase in systolic and diastolic blood pressure were 1.09 (95% CI: 1.03–1.16) and 1.19 (95% CI: 1.10–1.28), respectively.

The joint associations of gestational hypertension and hypertension at the inter-conception examination with the risks of diabetes and pre-diabetes are shown in Fig. 1. The relative risk of having type 2 diabetes was the highest among GDM women who had both gestational hypertension and hypertension at the inter-conception examination (OR: 7.12, 95% CI: 2.56–19.8), followed by women who

Table 3
Odds ratios for pre-diabetes by gestational hypertension and high blood pressure at the inter-conception examination.

	No. of participants*	Odds ratios (95% confidence intervals)		
		Model 1†	Model 2‡	Model 3§
History of gestational hypertension				
No	1110	1.00	1.00	1.00
Yes and not using antihypertensive drugs	49	1.36 (0.76–2.44)	1.40 (0.78–2.54)	0.94 (0.50–1.77)
Yes and using antihypertensive drugs	21	1.79 (0.75–4.26)	1.59 (0.66–3.84)	0.81 (0.31–2.08)
Systolic blood pressure categories				
<120 mmHg	978	1.00	1.00	1.00
120–129 mmHg	156	2.20 (1.56–3.10)	2.10 (1.48–2.98)	1.55 (1.07–2.23)
130–139 mmHg	26	4.36 (1.92–9.91)	4.01 (1.75–9.22)	2.35 (1.00–5.54)
≥140 mmHg	20	4.29 (1.69–10.9)	4.26 (1.65–11.0)	2.15 (0.79–5.87)
P for trend		<0.001	<0.001	0.020
Systolic blood pressure as a continuous variable (5 mmHg increase)		1.43 (1.28–1.59)	1.4 (1.26–1.57)	1.2 (1.06–1.35)
Diastolic blood pressure categories (%)				
<80 mmHg	809	1.00	1.00	1.00
80–84 mmHg	258	1.92 (1.43–2.56)	1.91 (1.42–2.56)	1.46 (1.07–1.99)
85–89 mmHg	39	2.21 (1.15–4.22)	2.02 (1.04–3.91)	1.41 (0.72–2.79)
≥90 mmHg	74	4.48 (2.72–7.38)	4.37 (2.63–7.24)	2.76 (1.62–4.69)
P for trend		<0.001	<0.001	0.001
Diastolic blood pressure as a continuous variable (5 mmHg increase)		1.72 (1.49–1.98)	1.69 (1.47–1.95)	1.42 (1.22–1.65)
Systolic/diastolic blood pressure categories				
<120/80 mmHg	766	1.00	1.00	1.00
120–129/80–84 mmHg	295	2.04 (1.54–2.70)	2.04 (1.53–2.71)	1.56 (1.16–2.11)
130–139/85–89 mmHg	43	1.94 (1.03–3.63)	1.75 (0.92–3.32)	1.12 (0.58–2.18)
≥140/90 mmHg	76	4.89 (2.97–8.04)	4.80 (2.90–7.96)	2.97 (1.75–5.05)
P for trend		<0.001	<0.001	<0.001

* Diabetes participants were excluded from this analysis.

† Adjusted for age.

‡ Adjusted for age, education, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, dietary fiber, total energy intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat.

§ Adjusted for variables in model 2 and also pre-pregnancy body mass index and baseline body mass index.

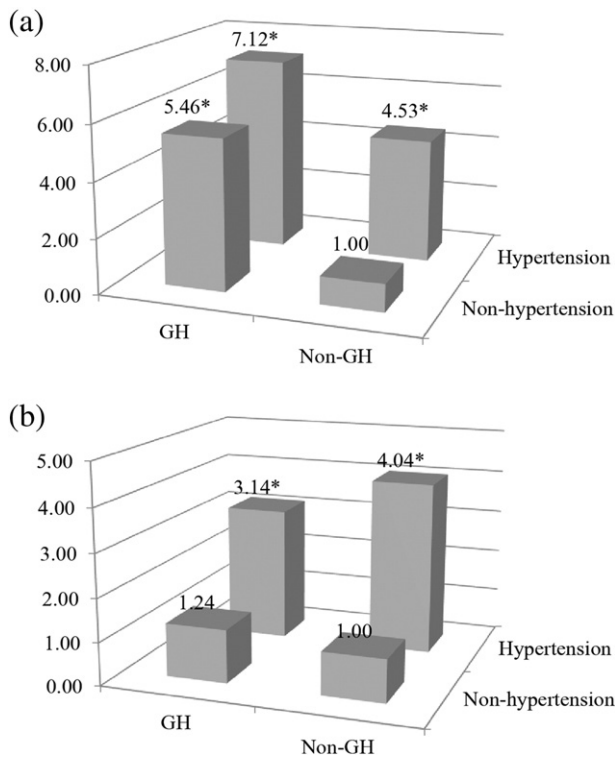


Fig. 1. Odds ratios of diabetes (a) and pre-diabetes (b) based on different status of gestational hypertension and hypertension at the inter-conception examination. Adjusted for age, education, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, dietary fiber, total energy intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, energy percent of saturated fat, pre-pregnancy body mass index, and baseline body mass index. GH = gestational hypertension; * $P < 0.05$.

had gestational hypertension alone (OR: 5.46, 95 CI%: 2.71–11.0) and hypertension at the inter-conception examination alone (OR: 4.53, 95 CI%: 2.23–9.22) compared with GDM women who had normal blood pressure both during pregnancy and at the inter-conception examination. The significantly increased risk of prediabetes was found among GDM women with hypertension at the inter-conception examination alone (OR: 4.04, 95 CI%: 2.30–7.11) and GDM women with both gestational hypertension and hypertension at the inter-conception examination (OR: 3.14, 95 CI%: 1.19–8.27). We did not find any interactions between gestational hypertension and hypertension at the inter-conception examination with the risks of type 2 diabetes and pre-diabetes.

4. Discussion

We found that both gestational hypertension in the index pregnancy and chronic hypertension at the inter-conception examination were significantly and independently associated with type 2 diabetes among women with prior GDM. Chronic hypertension at the inter-conception examination was independently associated with pre-diabetes among women with prior GDM.

Only a few prospective studies have assessed the association between gestational hypertension and the risk of type 2 diabetes. Several studies in Australia (Callaway et al., 2007), Denmark (Lykke et al., 2009), Canada (Feig et al., 2013), and Norway (Engeland et al., 2011) with long follow-up (3.7–21 years) have indicated that gestational hypertension has a 2–3.1 times high risk of type 2 diabetes. However, other studies conducted in Japan (Kurabayashi et al., 2013) and New York City (Savitz et al., 2014) did not find any association between gestational hypertension and type 2 diabetes risk. As women in the Japanese study were nurses, they may have

been healthier than the general population, introducing a selection bias. The New York study confirmed diabetes status only through hospital discharge diagnoses, which obviously missed many cases of diabetes treated outside hospital and all cases of asymptomatic diabetes. All these previous studies comprised pregnant women from the general population. Although women with GDM are more likely to have gestational hypertension than the general pregnant women, no study has evaluated the association between gestational hypertension and the risk of type 2 diabetes among women with prior GDM.

Our study also suggested that an association between high blood pressure at the inter-conception examination and the risks of type 2 diabetes and pre-diabetes existed among women with prior GDM. Several large prospective studies have demonstrated that high blood pressure is a prominent predictor of diabetes risk in adults (Lee et al., 2011; Wei et al., 2011). Additionally, a systematic review (Colosia, Palencia, & Khan, 2013) of 92 observational studies showed that hypertension is a common comorbidity in adults with type 2 diabetes, which is in keeping with our results. In the present study, there was no evidence of interaction between gestational hypertension and hypertension at the inter-conception examination with the risk of type 2 diabetes, although both of them were associated with type 2 diabetes risk.

The association between gestational hypertension and type 2 diabetes might be explained by obesity and insulin resistance. Pre-pregnancy obesity is associated with a higher risk of gestational hypertension (Li et al., 2013), as well as type 2 diabetes and pre-diabetes (Wang et al., 2014) among GDM women. In obese women, adipose tissue produces increased amounts of substances which include not only factors that contribute to the development of insulin resistance (Kahn, Hull, & Utzschneider, 2006) but also adipokines that lead to microvascular dysfunction (De Boer et al., 2012; Karaca, Schram, Houben, Muris, & Stehouwer, 2014). Microvascular dysfunction raises blood pressure (Karaca et al., 2014) and insufficient β -cell function accompanied by insulin resistance is key risk factor of diabetes (Kahn et al., 2006; Li et al., 2014). Notably, pre-pregnancy BMI and postpartum BMI are known risk factors of type 2 diabetes. Adjustment for pre-pregnancy BMI and postpartum BMI at baseline survey slightly attenuated the direct association between gestational hypertension and type 2 diabetes risk. However, the positive association still remained significant in the present study. We hypothesized that both obesity and insulin resistance independently contributed to the increased risk of diabetes in GDM women with a history of gestational hypertension.

There were several strengths in our study. First, the present study was the first population-based study focusing on the impact of gestational hypertension on the risks of diabetes and pre-diabetes in Chinese women with a history of GDM. This was the first study to test the interaction between gestational hypertension and chronic hypertension at the inter-conception examination for the risk of type 2 diabetes. Second, we used a 2-h 75-g OGTT to confirm type 2 diabetes and pre-diabetes referring to the criteria of American Diabetes Association (American Diabetes Association, 2009), and thus accurately ascertained the cases of incident diabetes. Limitations of this study included the retrospective nature of the cohort study, and self-reported gestational hypertension history that might introduce recall bias. Nevertheless, validation studies in the United States (Dietz et al., 2014) and England found good concordance between self-reported hypertensive disorder during pregnancy and clinical records. Although our original sample was representative of the total population of GDM women, we had a small sample size for women with pre-diabetes because of the low response rate at 27%, resulting in a large variation in estimates.

5. Conclusions

Both gestational hypertension and chronic hypertension at the inter-conception examination were associated to type 2 diabetes in women who had a history of GDM. These results provide evidence for

future randomized controlled trials to prevent type 2 diabetes in GDM women with hypertension during pregnancy. High blood pressure level should call healthcare providers' attention to prevent diabetes in women at risk during pregnancy.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.jdiacomp.2016.04.025>.

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