ORIGINAL ARTICLE

Higher blood pressure and heart rate are associated with a higher incidence of gestational diabetes mellitus in early pregnancy

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Objective. **To explore whether blood pressure and heart rate are risk factors for gestational diabetes mellitus (GDM) in early pregnancy, and to outline intervention strategies for managing GDM as soon as possible.** ***Methods.*** **This is a single center, cross-sectional study conducted from February to August 2019 in the first affiliated hospital of Soochow university. The data including the demographic and clinical data, 796 pregnant women during 8-12 weeks of gestation were analyzed.** ***Results.*** **The incidence of GDM in early pregnancy was 9.50%. The results of logistic regression analysis are as follows: systolic blood pressure≥110mmHg (OR 2.638, 95% CI 1.305-5.334, p = 0.007), heart rate≥80 beats/min (OR 2.146, 95% CI 1.214-3.794, p = 0.009), higher hemoglobin (OR 1.041, 95% CI 1.011-1.072, p = 0.007), multiparity (OR 1.749, 95% CI 1.053-2.906, p = 0.031), pre-pregnancy overweight or obesity (OR 2.850, 95% CI 1.661-4.889, p<0.001) and twin pregnancy (OR 3.768, 95% CI 1.195-11.883, p = 0.024) are the risk factors for GDM in early pregnancy.** ***Conclusion.*** **Systolic blood pressure≥110mmHg, heart rate≥80 beats/min, higher hemoglobin, multiparity, pre-pregnancy overweight or obesity and twin pregnancy are risk factors for GDM in early pregnancy.**

Key words: **Blood Pressure; Heart Rate; Gestational Diabetes Mellitus; Early Pregnancy.**

Objetivo. **Explorar si la presión arterial y la frecuencia cardiaca son factores de riesgo para la diabetes mellitus gestacional en el embarazo temprano, y destacar las estrategias para el manejo de esta entidad lo más pronto posible.** ***Métodos.*** **Este es un estudio transversal en un solo cetro hospitalario, realizado de Febrero a Agosto de 2019 en el primer hospital afiliado de la Universidad de Soochow. Se incluyen los datos demográficos y clínicos de 796 mujeres embarazadas entre 8 a 12 semanas de gestación que fueron analizados.** ***Resultados.*** **La incidencia de la diabetes mellitus gestacional en el embarazo temprano fue de 9.5%. Los resultados del análisis con regresión logística fueron: presión arterial sistólica ≥110 mmHg (OR 2.638, 95% CI 1.305-5.334, p = 0.007), frecuencia cardiaca ≥80 latidos/min (OR 2.146, 95% CI 1.214-3.794, p = 0.009), Hemoglobina más alta (OR 1.041, 95% CI 1.011-1.072, p = 0.007), multiparidad (OR 1.749, 95% CI 1.053-2.906, p = 0.031), obesidad o sobrepeso previos al embarazo (OR 2.850, 95% CI 1.661-4.889, p<0.001) y embarazo gemelar (OR 3.768, 95% CI 1.195-11.883, p = 0.024) son los factores de riesgo para el desarrollo de diabetes mellitus gestacional en el embarazo temprano.** ***Conclusión.*** **La presión arterial sistólica ≥110 mmHg, frecuencia cardiaca ≥80 latidos por minuto, Hemoglobina elevada, multiparidad, y la obesiad y sobrepeso previos al embarazo son factores de riesgo para la aparición de la diabetes mellitus gestacional en el embarazo temprano.**

Palabras clave**: Presión arterial; Frecuencia cardiaca; Diabetes mellitus gestacional; Embarazo temprano.**

Cir Card Mex 2020; 5(2): 28-33

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Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy and it is usually characterized by glucose intolerance first recognized during pregnancy [1]. Due to different screening strategies and diagnosis criteria, there were large differences between the global prevalence of GDM, which ranging from 1.8% to 25.1% [2]. GDM is associated with adverse maternal and neonatal outcomes, such as cesarean section, infection, neonatal hypoglycemia, macrosomia, neonatal severe respiratory distress syndrome and in-born nursery admissions [3-5]. After delivery, women with a history of GDM are at increased risk of developing type 2 diabetes mellitus (T2DM), cardiovascular disease, and are associated with metabolic syndrome, malignancies, ophthalmic and depression in the future [6-8]. In addition, the offspring of women with previous GDM are more likely to have T2DM, obesity, ophthalmic disease, long-term neuropsychiatric disease in the future [9-11]. Therefore, identifying and managing the risk factors for GDM is beneficial in reducing the incidence of GDM and maternal and neonatal outcomes.

Current diagnostic criteria for GDM are controversial, oral glucose tolerance test for GDM during 24-28 weeks of gestation is now generally recommended, but given increasing evidence showed that GDM screening can conducted at early pregnancy stage [12]. According to the International Federation of Gynecology and Obstetrics (FIGO) at any time during the course of pregnancy, women with fasting plasma glucose (FPG) in the range of 5.1-6.9 mmol/L could be diagnosed as GDM [1]. The study has shown that first-trimester FPG level is associated with pregnancy outcomes [13]. Importantly, lifestyle interventions commenced in early pregnancy can prevent the occurrence of GDM and adverse pregnancy outcomes [14-15]. So, early diagnosis of GDM and understanding the risk factors are beneficial to pregnant women, by enabling them to effectively manage their blood glucose and reduce adverse pregnancy outcomes.

In addition, some studies have suggested that blood pressure is associated with the incidence of GDM. A study reported that higher systolic blood pressure (SBP) and diastolic blood pressure (DBP) were risk factors for GDM, and a 10-mmHg rise in SBP and DBP increased the relative risk of GDM by 49% and 34%, respectively [16]. Two studies in Xiamen and Tianjin, China showed that SBP associated with GDM incidence [17-18]. A study from Canada showed that DBP ≥80 mmHg in early pregnancy was risk factors for GDM.19 However, the diagnosis of GDM in these studies were during 24-28 weeks of gestation, we want to explore the relationship between blood pressure and the incidence of GDM in early pregnancy. In addition, some studies have suggested that heart rate (HR) may has a link with diabetes, but the extent of its association with GDM remains unknown [19-22]. So, the purpose of this study is to explore whether BP and HR are the risk factors for GDM in early pregnancy and to outline intervention strategies for managing GDM as soon as possible.

MATERIAL

Materials design and sample

This was a cross-sectional study of pregnant women conducted at the first affiliated hospital of Soochow university, China, from February to August 2019. Participants were eligible for inclusion if gestational age was 8-12 weeks and they volunteered to participate in this study. Exclusion of participants was based on a history of diabetes or other chronic diseases, absence of FPG screening in early pregnancy.

Demographic and clinical data

The socio-demographic information included gestational age and menarche age; marital, working, income and educational statuses; sleep, dietary behavior and exercise during pregnancy; smoking and alcohol abuse. Pregnancy related data including (1) gestational age, parity, planned pregnancy, mode of conception, early pregnancy response, history of macrosomia and complicated pregnancy, polycystic ovary syndrome (PCOS); (2) pre-pregnancy body mass index (BMI), SBP, DBP, HR ; (3) family history (first degree) of diabetes, a history of GDM; (4) some biomarkers measured in the first trimester were containing hemoglobin, blood uric acid, leukocyte count, alanine aminotransferase, thyroid stimulating hormone.

Measurement of variables

HR and BP: Before measurements were carried out, the women did not exercise vigorously and drink coffee. They were kept relaxed. The researcher measured BP and HR of the right upper arm with electronic sphygmomanometer (HBP-9020, Omron, Japan).

Depression: Two items on the Patient Health Questionnaire, "little interest or pleasure in doing things" and "feeling down depressed, or hopeless" in the past two weeks were used to assess the women's level of depression. For each item, the options were "not at all, several days, more than half the days, and nearly every day", and the scores were "0, 1, 2, and 3", respectively. The cut off point of ≥ 3 was used to identify depression (range 0 to 6) [23].

Biomarkers: The data on biomarkers in the first trimester were extracted from Haitai Electronic Medical Record System by using the pregnant women's clinic numbers.

Diet behavior during pregnancy: Diet behavior during pregnancy was measured by GDM diet behavior questionnaire which was developed by our team in December 2018. It contains 3 scales and 16 items. The content validity index of the questionnaire is 0.972, the Cronbach's alpha coefficient is 0.802, and the test-retest reliability is 0.849. The first dimension focused on examining diet status in terms of choosing low glycemic index (GI) and high GI foods; the second dimension was based on examining the frequency of intake of different food categories; the last dimension involved evaluating the intake of the total quality of foods and staple food. The total score is from -15 to 70 points. The higher the score, the healthier dietary behavior pregnant woman has.

Diagnosis of GDM

The diagnose of GDM at early pregnancy stage adopt FIGO diagnostic criteria : participants whose FPG was 5.1-7.0 (mmol/L) at any time was diagnosed as GDM.

All women were informed not to eat and drink after 8 pm on the day before testing. FPG was measured at about 12 weeks of gestational. The process involved the collection of 1.5 ml venous blood which was placed in the serum separation tube, and centrifuged at 3000 r/min for 10 min. Plasma glucose levels were measured using a hexokinase enzymatic reference method (C1-6000, Abbott Laboratories, USA).

Table 1. Demographic and clinical data for pregnant women, N=796, n (%) /Mean ± SD

	GDM			
	Yes	No	*x/t*	*p value*
Gestational age (years)			4.223	0.040
< 35	665(91.1)	65(8.9)		
≥ 35	55(83.3)	11(16.7)		
Working status			2.946	0.086
Housewife	613(91.2)	59(8.8)		
Job	107(86.3)	17(13.7)		
Educational status			1.907	0.167
Junior middle school and below	338(88.9)	42(11.1)		
Senior high school and above	382(91.8)	34(8.2)		
Living area			0.729	0.393
Urban	631(90.8)	64(9.2)		
Rural	89(88.1)	12(11.9)		
Inspection cost			0.032	0.858
Medical insurance	584(90.5)	61(9.5)		
Self-pay	136(90.1)	15(9.9)		
Personal monthly income (yuan)			2.349	0.125
<5000	267(88.4)	35 (11.6)		
≥5000	453(91.7)	41(8.3)		
Marital status			0.144	0.449
Married	700(90.3)	75(9.7)		
Single/divorced/widowed	20(100.0)	1(0.0)		
Pre-pregnancy BMI(Kg/m2)			25.916	0.000
<24	624(92.7)	49(7.3)		
≥24	96(78.0)	27(22.0)		
Exercise during pregnancy			1.276	0.259
Never or seldom	562(91.1)	55(8.9)		
Often	158(88.3)	21(11.7)		
Depression during pregnancy			0.023	0.881
No	477(90.3)	51(9.7)		
Yes	243(90.7)	25(9.3)		
Times of pregnancy			3.139	0.076
1	342(92.4)	38(7.6)		
≥2	378(88.7)	48(11.3)		
Parity			3.309	0.069
Primiparity	491(91.8)	44(8.2)		
Multiparity	229(87.7)	32(12.3)		
Planned pregnancy			0.339	0.560
No	488(90.0)	54(10.0)		
Yes	232(91.3)	22(8.7)		
Mode of conception			0.414	0.036
Natural	652(91.2)	63(8.8)		
Ovulation/ Artificial test tube	68(84.0)	13(16.0)		
Fetus number			5.760	0.016
Singleton pregnancy	708(90.9)	71(9.1)		
Twin pregnancy	12(70.6)	5(29.4)		

Early pregnancy response			**3.442**	**0.064**
No	**172(94.0)**	**11(6.0)**		
Yes	**548(89.4)**	**65(10.6)**		
Family history of diabetes (first degree)			**1.514**	**0.218**
No	**664(90.8)**	**67(9.2)**		
Yes	**56(86.2)**	**9(13.8)**		
History of GDM			**0.792**	**0.135**
No	**714(90.6)**	**74(9.4)**		
Yes	**6(75.0)**	**2(25.0)**		
History of polycystic ovary syndrome			**4.509**	**0.034**
No	**683(91.1)**	**67(8.9)**		
Yes	**37 (80.4)**	**9(19.6)**		
History of macrosomia			**0.195**	**0.659**
No	**699(90.3)**	**75(9.7)**		
Yes	**21(95.5)**	**1(4.5)**		
History of bad pregnancy			**0.546**	**0.460**
No	**571(90.1)**	**63(9.9)**		
Yes	**149(92.0)**	**13(8.0)**		
Systolic blood pressure (mmHg)			**10.537**	**0.001**
<110	**223(95.7)**	**10(4.3)**		
≥110	**497(88.3)**	**66(53.8)**		
Diastolic blood pressure (mmHg)			**11.375**	**0.001**
<70	**315(94.6)**	**18(5.4)**		
≥70	**405(87.5)**	**58(12.5)**		
Heart rate (beats/min)			**10.648**	**0.001**
<80	**310(94.5)**	**18(5.5)**		
≥80	**410(87.6)**	**58(12.4)**		
Menarche age (years)	**13.78±1.29**	**13.79±1.31**	**-0.093**	**0.926**
Sleep duration in pregnancy (hour)	**8.69±1.65**	**8.89±1.26**	**-1.004**	**0.315**
Hemoglobin (g/L)	**127.68±8.82**	**130.95±9.00**	**-3.068**	**0.002**
Blood uric acid (μmol/L)	**210.78±45.20**	**213.07±42.70**	**-0.423**	**0.673**
Leukocyte count (10^9/L)	**8.70±1.98**	**8.91±2.01**	**-0.882**	**0.380**
Alanine aminotransferase (U/L)	**20.09±15.72**	**22.27±14.82**	**-1.153**	**0.249**
Thyroid stimulating hormone (mIU/L)	**1.77±1.19**	**1.65±1.46**	**0.834**	**0.405**
Dietary behavior (score)	**35.22±8.81**	**35.97±8.34**	**-0.717**	**0.474**

BMI = body mass index; GDM= gestational diabetes mellitus.

Procedures

One investigator collected information using a general questionnaire. Before the questionnaire was filled in, the participants were informed of the purpose of this study and confidentiality of information, and having the right to refuse to participate in this study. All participants signed informed consent form. Before the participants filled in the questionnaire, the researcher spoke to them in clear language and answered their questions during the survey. It took 15-25 minutes to complete the questionnaire. After completing the survey, the researcher checked whether all the items on the questionnaire were complete. The data relating to FPG in the first trimester were extracted from Haitai Electronic Medical Record System by using the pregnant women's clinic number.

Ethical Approval

The study was approved by the Ethics Committee of the first affiliated hospital of Soochow university (No.2018175).

Statistical Analysis

The demographic and clinical data were expressed as the means ± standard deviations for continuous variables and numbers (percentages) for categorical variables. T-tests were carried out for continuous variables and chi-square tests or Fisher's exact analysis for categorical variables. All variables with $p < 0.1$ in univariate analysis were included as independent variables. The incidence of GDM was used as dependent variable. Odds ratio (OR) and 95% Confidence interval (CI) were examined as part of the statistical analysis. Data were analyzed using SPSS 20.0 software (SPSS, Inc. Chicago, IL). All of the tests were two-tailed, and $p < 0.05$ was though t to be statistically significant.

RESULTS

Of the 900 eligible participants, 2 of them missed more than 25% of the information in the questionnaire, 102 did not

Table 2. Risk factors associated with the occurrence of gestational diabetes mellitus

VARIABLE	COEFFICIENT	OR *(95% CI)*	*p value*
Systolic blood pressure (mmHg) (ref: <110)	**0.970**	**2.638(1.305,5.334)**	**0.007**
Heart rate (beats/min) (ref: <80)	**0.764**	**2.146(1.214,3.794)**	**0.009**
Hemoglobin (g/L)	**0.040**	**1.041(1.011,1.072)**	**0.007**
Parity (ref: primiparity)	**0.559**	**1.749(1.053,2.906)**	**0.031**
Pre-pregnancy BMI (Kg/m2) (ref: <24)	**1.047**	**2.850(1.661,4.889)**	**<0.001**
Fetus number (ref: 1)	**1.327**	**3.768(1.195,11.883)**	**0.024**
Constant	**-9.205**	**0.000**	**<0.001**

have FPG in early pregnancy. The incidence of GDM in early pregnancy is 9.50%. The results of univariate analysis showed that gestational age, working status, pre-pregnancy BMI, times of pregnancy, parity, mode of conception, fetus number, early pregnancy response, history of PCOS, hemoglobin, SBP, DBP and HR were significantly ($p<0.05$) associated with the occurrence of GDM in early pregnancy **(Table 1)**.

Multiple stepwise regression analysis indicated that SBP≥110mmHg (OR 2.638, 95% CI 1.305-5.334, p=0.007), HR≥80 beats/min (OR 2.146, 95% CI 1.214-3.794, p=0.009), higher hemoglobin (OR 1.041, 95% CI 1.011-1.072, p=0.007), multiparity (OR 1.749, 95% CI 1.053-2.906, p=0.031), pre-pregnancy overweight or obesity (OR 2.850, 95% CI 1.661-4.889, p<0.001) and twin pregnancy (OR 3.768, 95% CI 1.195-11.883, p=0.024) are the risk factors for GDM in early pregnancy (**Table 2**).

DISCUSSION

Our study uses FIGO's diagnostic criteria for GDM in early pregnancy. The incidence of GDM in this study in early pregnancy is 9.5%, which is similar to a study on the incidence of GDM (about 10%) in early pregnancy in Iran [24]. No other studies was found to report the incidence of GDM in early stage.

Studies have shown that pregnant women with chronic hypertension are at higher risk of developing GDM [25]. This may be due to women with hypertension has more insulin resistant [26]. As consistent with our hypothesis, women with SBP ≥ 110mmHg, have 2.638-fold increase in the risk of developing GDM than those were SBP ≥ 110 mmHg, which was consistent with Yan's and Junhong's researches [17,18].

The increased HR represented the imbalance of central nervous system activity, associated with increased sympathetic nervous system (SNS) activity, which would lead to vasoconstriction, reduced blood flow in skeletal muscle, and impaired skeletal muscle glucose uptake [27]. SNS overactivity might stimulate the renin–angiotensin–aldosterone system (RAAS), which conversely causes increased HR and insulin resistance. Higher HR has been shown to be associated with increased CRP levels and subclinical inflammation represented by white blood cell counts, while insulin resistance and subclinical inflammation were associated with the development of GDM [28]. Therefore, increased heart rate may be one of the risk factors for GDM. This study found that the participants with a HR ≥ 80 beats/min had a higher GDM risk with 2.146 times than those with a HR < 80 beats/min, which confirmed our hypothesis.

The higher rate of GDM would lead to an increase of maternal and child adverse outcomes. Therefore, it is particularly important to find the risk factors for GDM in early pregnancy. Similarly, as in the previous studies, we found some classic risk factors of GDM such as hemoglobin, multiparity, pre-pregnancy overweight or obesity, and twin pregnancy are to be significantly associated with GDM. Study by Chen Wang showed an association between GDM and hemoglobin [29,30]. Women with multiparity have also been found to have a higher prevalence of GDM compared to those with primiparity [31,32]. Many previous studies and some guides to GDM have demonstrated that pre-pregnancy overweight or obesity was an important risk for GDM, which are similar to the findings of the current study [33,34]. Twin pregnancy have also been found to have a higher prevalence of GDM compared to those with singleton pregnancy [35].

One of the limitations of this study was the findings which demonstrated an association between some clinical indicators and the incidence of GDM was based on a cross-sectional study. We need more prospective cohort studies to confirm the result.

FUNDING: This work was supported by the Suzhou Science and Technology Project, China under Grant number SYS2019026.

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

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