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Original Article

The association of maternal ABO blood group with gestational diabetes mellitus in Japanese pregnant women

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ABSTRACT

Aims: To investigate the association between the ABO blood group and gestational diabetes mellitus (GDM).

Materials and methods: A retrospective case–control study was conducted using data from 5424 Japanese pregnancies. GDM screening was performed in the first trimester using a casual blood glucose test and in the second trimester using a 50-g glucose challenge test. If the screening was positive, a 75-g oral glucose tolerance test was performed for a GDM diagnosis, which was defined according to the International Association of Diabetes and Pregnancy Study Groups. Logistic regression was used to obtain the odds ratio (OR) and 95% confidence interval (CI) adjusted for traditional risk factors.

Results: Women with the A blood group (adjusted OR: 0.34, 95% CI: 0.19–0.63), B (adjusted OR: 0.35, 95% CI: 0.18–0.68), or O (adjusted OR: 0.39, 95% CI: 0.21–0.74) were at decreased risk of GDM compared with those with group AB. Women with the AB group were associated with increased risk of GDM as compared with those with A, B, or O (adjusted OR: 2.73, 95% CI: 1.64–4.57).

Conclusion: ABO blood groups are associated with GDM, and group AB was a risk factor for GDM in Japanese population.

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1. Introduction

The ABO blood group system is a classification of blood types based on the presence or absence of A and B antigens on red blood cells; it is the most generally used blood group classification in clinical practice. Recently, some studies have reported associations between particular ABO phenotypes and an increased susceptibility to certain diseases including infection [1], cancer [2], vascular disease [3], and dementia [4].

A few studies have examined the possible associations between ABO blood groups and the risk of type 2 diabetes mellitus (T2DM). Two studies, one from Malaysia [5] and the other from India [6] have reported higher frequencies of the B group among patients with T2DM. On the other hand, in Nigerian subjects, the O (Rh negative) and A groups (Rh positive) were significantly higher

among diabetic subjects than controls [7]. A prospective cohort study consisting of 82,104 women reported that groups A and B were at increased risk of T2DM compared with the O group [8]. Although some studies showed a link between ABO blood group and T2DM, the associations were not observed in others [9,10].

Gestational diabetes mellitus (GDM) is defined as glucose intolerance, which initiates or is diagnosed during pregnancy. This disorder is a common medical problem presenting increased risks of complications for both mother and child during pregnancy. In contrast with T2DM, literatures concerning the association of ABO blood types with GDM are scarce. In Turkish subjects, Karagoz et al. reported a higher risk of GDM in the AB group patients [11]. However, this finding is in contrast with a Chinese study that reported AB group was less likely to correlate with GDM [12]. Furthermore, a retrospective cohort study conducted in Thailand showed that the ABO blood group was correlated with preeclampsia, but not with GDM [13]. The discrepancy in the results from these studies may be partly due to the variation in the genetic profiles among different ethnic groups. The aim of the present study was to determine whether the ABO blood group has an association with GDM in the Japanese population.

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2. Materials and methods

2.1. Study population

Between October 2010 and September 2015, 5864 pregnancy women delivered at the Obstetrics Department of Iida Municipal Hospital, Nagano, Japan. In the present retrospective study, we collected information from the birth register. Cases with known type 1 or type 2 diabetes, taking medications affecting glucose metabolism, missing information on maternal height or weight, random glucose levels, and ABO blood groups were excluded. Women who had a fetus with a chromosomal or congenital abnormality were also excluded. To eliminate any possible bias arising from including the same woman more than once, we used the date of most recent delivery if a woman had delivered twice or more in the hospital.

2.2. GDM screening and definitions

Based on the clinical recommendation by the Japan Society of Obstetrics and Gynecology [14], all women underwent a universal two-step screening for GDM. In the first trimester the casual blood glucose test with a cutoff value of 100 mg/dL was used, and in the second trimester a non-fasting 50-g blood glucose challenge test with a cutoff value of 140 mg/dL was used. If the screening was positive, a 75-g oral glucose tolerance test (OGTT) after an overnight fast was performed for the definite diagnosis of GDM. Overweight or obese women were recommended to undergo a 75-g OGTT at any time during gestation. GDM was defined according to the International Association of Diabetes and Pregnancy Study Groups [15] and the American Diabetes Association criteria [16] at a plasma glucose concentration equal or higher than one of the three following cut off points: (1) baseline, 92 mg/dL; (2) 1-h post OGTT, 180 mg/dL; or (3) 2-h post OGTT, 153 mg/dL. Informed consent was obtained from all participants. Informed consent was obtained from all participants.

Pre-gestational weight was self-reported at the first prenatal visit. Information on behavioral factors and familial history of diabetes were collected through interviews. Habitual smokers were subjects who continuously smoked one or more cigarettes per day for at least six months before pregnancy. Habitual drinkers were those who consumed liquor on four or more occasions per month before pregnancy. Subjects consuming anti-hypertensive agents before pregnancy, or having a blood pressure of >140/90 mmHg on more than two occasions before 20 weeks of gestation, were defined as those with chronic hypertension [17]. Subjects with a familial history of diabetes had one or more first degree diabetic relatives.

2.3. Laboratory analysis

Plasma glucose samples collected in fluoride oxalate tubes were assessed within 2 h of sampling using the hexokinase method (GLU-HK; Shinotest Inc., Kanagawa, Japan). The ABO blood group was evaluated via agglutination technology using the Ortho[®] BioVue system (Ortho Clinical Diagnostics Japan, Tokyo, Japan) in the hospital.

2.4. Statistical analysis

To compare the difference between the GDM and non-GDM groups, the Student's *t*-test was used for continuous variables, and chi-squared test or Fisher's test was used to compare the categorical parameters. Binary logistic regression analysis was performed to obtain the odds ratio (OR) and 95% confidence interval (CI) of ABO groups for GDM using both univariable and

multivariable analysis. In multivariable analysis, traditional risk factors for GDM including maternal age, pre-pregnancy body mass index (BMI), parity, chronic hypertension, non-singleton pregnancy, and familial history. Data are expressed as mean \pm standard deviations. *P* values <0.05 were considered statistically significant. Statistical analyses were performed using the SPSS software version 21.0 (SPSS Inc., IL, USA).

3. Results

Of the 5484 women who visited Iida Municipal Hospital for delivery between January 2010 and September 2015, 5424 were included in the present study. Of the women included in analyses, 149 (2.75%) were diagnosed with GDM (Table 1). Compared with the non-GDM group, maternal age and pre-pregnancy BMI, frequency of multiparity, chronic hypertension, and familial history of diabetes were significantly higher among GDM group. Among the 5275 non-GDM subjects, the A, B, O, and AB blood groups were 1999 (37.9%), 1250 (23.7%), 1507 (28.6%), and 519 (9.8%), respectively, which were similar to those frequencies reported previously for the Japanese general population (A, 38.7%; B, 22.2%; O, 29.3%; and AB, 10.0%) [18]. The distribution of blood groups was significantly different between the non-GDM and GDM subjects; women with GDM were more likely to have the AB blood group.

The clinical and biochemical characteristics of subjects according to the ABO blood group are shown in Table 2. Maternal age, pre-pregnancy BMI, random glucose level, frequency of multiparity, singleton pregnancy, chronic hypertension, and familial history of diabetes were similar among the four blood groups. In the univariable analysis, women with A, B, and O blood groups were at a decreased risk for GDM; their ORs versus the AB blood group were 0.42 (95% CI 0.26–0.66), 0.52 (95% CI 0.32–0.83), and 0.49 (95% CI 0.31–0.78), respectively (Table 3, Model M₀). Compared with the non-AB group, the AB group had a significant increased risk of GDM (OR 2.23, 95% CI 1.46–3.36). Furthermore, similar results were obtained from adjusted models for covariates

Table 1
Clinical and biochemical characteristics of subjects with non-GDM and GDM.

	Non-GDM	GDM	<i>P</i>
Number of subjects	5275	149	
Age (years)	30.7 \pm 4.9	33.6 \pm 5.4	<0.001 ^a
<30 (%)	2184 (41.4)	31 (20.8)	<0.001 ^b
31–34 (%)	1885 (35.7)	51 (34.2)	
\geq 35 (%)	1206 (22.9)	67 (45.0)	
Body height (cm)	159.1 \pm 4.0	157.9 \pm 6.4	0.755 ^a
Pre-pregnancy BMI (kg/m ²)	20.7 \pm 5.5	23.8 \pm 5.5	<0.001 ^a
Random glucose level (mg/dL)	80.9 \pm 7.0	85.4 \pm 14.3	<0.001 ^a
Parity \geq 1 (%)	2748 (52.1)	99 (66.4)	<0.001 ^b
Singleton pregnancy (%)	5117 (97.0)	149 (100.0)	0.011 ^b
Hypertension (%)	132 (2.5)	19 (12.8)	<0.001 ^b
Familial history of diabetes (%)	301 (5.7)	28 (18.8)	<0.001 ^b
Smoker (%)	232 (4.4)	8 (5.4)	0.330 ^b
Alcohol drinker (%)	380 (7.2)	7 (4.7)	0.157 ^b
ABO blood type (%)			
A	1999 (37.9)	45 (30.2)	0.001 ^b
B	1250 (23.7)	35 (23.5)	
O	1507 (28.6)	40 (26.8)	
AB	519 (9.8)	19 (19.5)	
Rh blood type (%)			
Positive	5250 (99.5)	149 (100.0)	0.400 ^b
Negative	25 (0.5)	0 (0.0)	

GDM; gestational diabetes mellitus, BMI; body mass index. Data are shown in mean \pm standard deviation or number (%).

^a Derived from Student's *t*-test.

^b Derived from χ^2 test or Fisher's exact test.

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