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Association between serum arsenic levels and gestational diabetes mellitus: A population-based birth cohort study

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ABSTRACT

Gestational diabetes mellitus (GDM) is a common obstetric complication with adverse effects on both mothers and their children. Previous studies revealed the link between Arsenic (As) exposure and incidence of diabetes mellitus (DM), but the data on the association between maternal As exposure and GDM is scarce. We examined this association among a population-based birth cohort. As concentrations were determined at multiple time points during pregnancy by ICP-MS. The association between As levels and GDM prevalence was examined using logistic regression model after adjustment for confounders. A total of 419 (12.85%) women were diagnosed with GDM. The incidences of GDM gradually increased with increasing quartiles of As levels with significant trend. As levels were associated with the GDM (95%CI: 1.29–2.43) at only the 4th quartile in the first trimester. After adjustment for maternal age, prepregnancy body mass index (BMI), monthly income, gestational age and parity, the association remains significant (95%CI: 1.22–2.38). Stratified analyses showed the associations were largely limited to normal maternal age (95%CI: 1.19–3.04) and normal weight women (95%CI: 1.18–2.66). Our study showed an association between As and GDM in a birth cohort and explored first trimester may be the critical period for As associated GDM. This association was universal in the general pregnant population of normal age and of normal weight.

1. Introduction

Gestational diabetes mellitus (GDM) is a major obstetric complication, defined as any degree of the impaired carbohydrate metabolism with onset or first recognition during pregnancy (Cruz-Hernández et al., 2016). The incidence of GDM ranges from 1% to 14% and has been increasing globally (Lavery et al., 2017; Cruz-Hernández et al., 2016). Hyperglycemia in pregnancy is associated with adverse effects for both mothers and their children (Sellers et al., 2016). GDM women have higher risks for cesarean, macrosomia, shoulder dystocia, and neonatal hypoglycemia at delivery (Billionnet et al., 2017). Moreover, both GDM mothers and their children are at higher risk of type 2 diabetes mellitus (DM), cardiovascular diseases, and metabolic syndromes in their later lives (Zhao et al., 2016; Hwu et al., 2016; Retnakaran and Shah, 2017). Although maternal age, maternal obesity, maternal inflammation and oxidative stress have been identified as potential risk factors, the underlying mechanisms and the exact etiology for GDM remain unknown (Lavery et al., 2017; Retnakaran, 2016).

Bizon et al. (2016) found the association between environmental pollutants such as heavy metals and the pathogenesis and progression of DM. Arsenic (As), known for its carcinogenic effect, is a widespread toxic heavy metal to which individuals are exposed primarily via contaminated drinking water (Farzan et al., 2013; Sandoval-Carrillo et al., 2016). Previous studies revealed the link between As exposure and increased incidence of DM (Navas-Acien et al., 2008; Grau-Pérez et al., 2017; Maull et al., 2012; Feseke et al., 2015; Liu et al., 2016; Wang et al., 2014; Kim et al., 2013). Several

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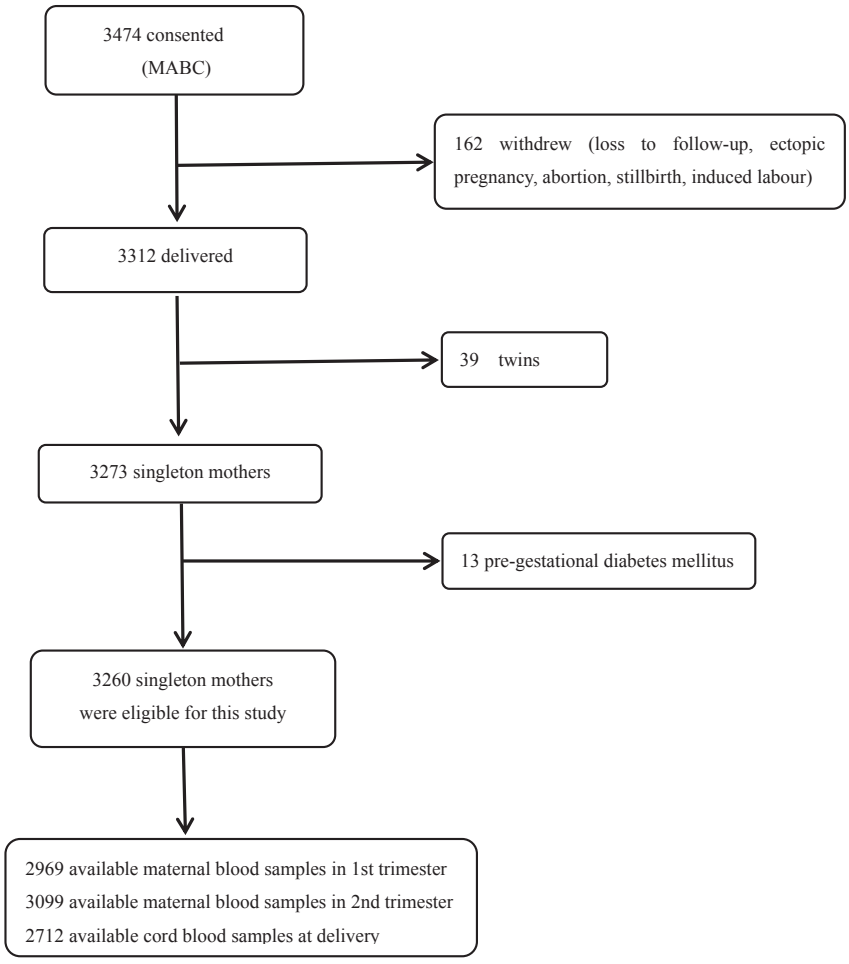

Fig. 1. Flow diagram of recruitment, follow-up, and identification of serum As in the Ma'anshan Birth Cohort (MABC).

mechanisms have been proposed on how As could affect glucose homeostasis, including insulin metabolism, oxidative stress, epigenetic effects and the disruption of the growth hormone/insulin-like growth factor axis (Andra et al., 2013; Padmaja et al., 2015; Douillet et al., 2013; Bailey et al., 2013; Palacios et al., 2012). Further, pregnant women may be vulnerable to toxic harmful effects (Rahman et al., 2016). There are limited studies on the association of maternal As exposure with GDM. Ettinger et al. (2009) collected maternal blood at delivery and reported that the risk of impaired glucose tolerance was higher among women with highest quartile of blood arsenic concentrations compared with those of the lowest quartile. Shapiro et al. (2015) reported a significant dose-response relationship between maternal blood arsenic level and risk of GDM ($p < .01$) in the first trimester from MIREC study. Farzan et al. (2016) observed that each 5 μg/L increase in As level in home well water correlated with a 10% higher odds of GDM. In a nested case-control study conducted by Peng et al. (2015), it is concluded that As in meconium was associated with GDM risk. In most of these studies, As exposure was measured in water, urine, toenail, meconium sample or was measured at one spot time. Therefore, whether maternal As exposure throughout pregnancy is associated with GDM needs further study.

There are two objectives in our study: 1) to explore the association between blood As levels and the risk of GDM at different gestational stages in a birth cohort; 2) to assess whether this association differed by maternal age and pre-pregnancy BMI and to

Table 1
Demographic characteristics of 3260 participants in MABC.

Maternal characteristics	GDM(n = 419)	Normal (n = 2841)	*P*
Age, y	27.79 ± 4.25	26.18 ± 3.48	<.001
≤24 y, n (%)	92 (21.96)	982 (34.56)	<.001
25–29 y, n (%)	207 (49.40)	1434 (50.48)	
≥30 y, n (%)	120 (28.64)	425 (14.96)	
Prepregnancy BMI, kg/m^2	21.92 ± 3.19	20.40 ± 2.64	<.001
<18.5, n (%)	52 (12.41)	680 (23.94)	<.001
18.5–23.9, n (%)	276 (65.87)	1905 (67.05)	
24–27.9, n (%)	73 (17.42)	214 (7.53)	
≥28, n (%)	18 (4.30)	42 (1.48)	
Gestational age, week	38.60 ± 1.66	39.09 ± 1.33	<.001
Parity, n (%)			
Nulliparous	357 (85.20)	2531 (89.09)	.020
Multiparous	62 (14.80)	310 (10.91)	
Gravidity, n (%)			
Primigravida	221 (52.74)	1580 (55.61)	.270
Multigravida	198 (47.26)	1261 (44.39)	
Monthly income, n (%)			
<1000yuan	7 (1.67)	47 (1.65)	.003
1000-2500yuan	126 (30.07)	686 (24.15)	
2500-4000yuan	179 (42.72)	1215 (42.77)	
>4000yuan	107 (25.54)	893 (31.43)	
Education			
≤High school	187 (44.63)	1204 (42.38)	.385
≥College	232 (55.37)	1637 (57.62)	
Newborn sex, n (%)			.786
male	211 (50.36)	1451 (51.07)	
female	208 (49.64)	1390 (48.93)	