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Maternal urinary triclosan level, gestational diabetes mellitus and birth weight in Chinese women

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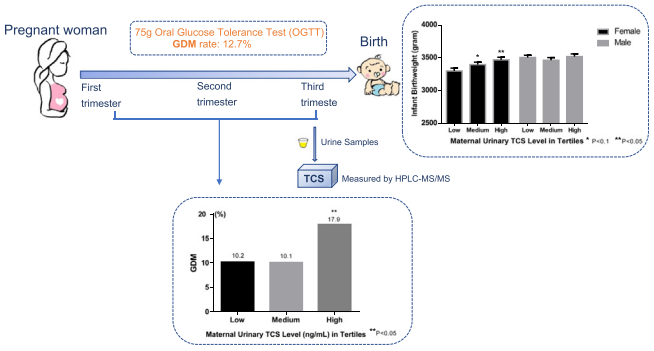
HIGHLIGHTS

- Triclosan (TCS) was detectable (> 0.1 ng/mL) in 97.9% of Chinese pregnant women.
- Maternal TCS exposure is associated with higher risk of gestational diabetes mellitus, which may partially intermediated via maternal BMI.
- Maternal TCS exposure is associated with higher birthweight among female infants.

GRAPHICAL ABSTRACT



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ABSTRACT

Triclosan (TCS) is an antibacterial chemical widely used in personal-care products and an endocrine disruptor. While TCS exposure is associated with insulin resistance and metabolic disorders in animals, few studies have assessed its effect on the risk of gestational diabetes mellitus (GDM) in humans. This study aimed to explore whether maternal urinary TCS level is associated with the risk of GDM and infant birthweight. We examined 620 pregnant women from Shanghai, China in 2012–2013. Urinary TCS level was measured with high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS), and categorized into high, medium and low in tertiles. GDM was defined based on recommendation of International Association of Diabetes and Pregnancy Study Groups (IADPSG). The GDM rate was 12.7%. TCS was detectable (≥0.1 ng/mL) in 97.9% women (median 2.7 ng/mL). There was a positive, but statistically non-significant association between urinary TCS levels and GDM (adjusted odds ratio 1.17; 95%CI: 0.99, 1.39, with each unit increase of log (TCS) ng/mL) with adjustment for urinary creatinine, maternal age, education, passive smoking, parity and prepregnancy BMI categories. 48.1% of infants were females. Birthweight was 122.8 g higher (95% CI: 13.9, 231.6 g) for female infants of women in high TCS (median 13.3 ng/mL) versus low TCS (median 0.77 ng/mL), with adjustment for urinary creatinine, prepregnancy BMI, GDM and other confounders. No association was found between maternal TCS and birthweight in male infants. These results suggested the potential for TCS to be associated with increased risk of GDM and a gender-specific association with higher birthweight among female infants in a population with widespread but moderate exposure to TCS.

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1. Introduction

Triclosan (TCS), a broad-spectrum antimicrobial chemical, has been widely used in personal-care products (toothpaste, mouthwash, antibacterial soap, hand sanitizer and cosmetics), clothing and plastics for >40 years (Jones et al., 2000). The common commercial use of TCS has resulted in its ubiquitous presence in the environment, as well as its continuous exposure of various populations (Meeker et al., 2013), including pregnant women (Meeker et al., 2013; Frederiksen et al., 2014; Bertelsen et al., 2014; Casas et al., 2011; Philippat et al., 2012; Wolff et al., 2008; Weiss et al., 2015). In our recent study, 98.2% of urine samples had detectable TCS (≥0.1 ng/mL) (Wang et al., 2017). Absorbed TCS in human body is mainly excreted via urine (Krishnan et al., 2010).

TCS is an endocrine disruptor chemical (EDC) with estrogenic/androgenic and thyroid hormone properties (Stoker et al., 2010; Gee et al., 2008). Animal studies show that TCS exposure induced insulin resistance and metabolic disorder (Regnault et al., 2016). In addition, maternal triclosan exposure was associated with increased plasma glucose, cholesterol, and triglycerides (Rabaglino et al., 2016). There are increasing concerns of EDCs being risk factors for gestational diabetes mellitus (GDM), due to biological plausibility (Ehrlich et al., 2016). The activation of estrogen receptors (ERs) may disrupt energy balance, fat and glucose metabolism (Ropero et al., 2008; Akahori et al., 2008). In addition, TCS was found to be associated with decreased free thyroxine (FT4) levels in women (Geens et al., 2015). The level of FT4 was inversely associated with incidence of GDM (Yang et al., 2016). However, no previous study examined the effect of maternal TCS exposure on GDM (Ehrlich et al., 2016).

In the past two decades, the incidence of GDM has increased dramatically around world (Coustan et al., 2010). The GDM incidence was found to be 18% on average in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, a large multinational cohort study (Sacks et al., 2012). GDM affects about 18% of pregnancies in China, which has a profound impact on programming offspring metabolic disorders in local population (Yang et al., 2009; Wei et al., 2014). This study aimed to fill in the knowledge gap on whether TCS affects glucose metabolism and occurrence of GDM.

A few studies have examined the association between prenatal TCS and birth weight in industrialized countries where the exposures of TCS were relatively high and the results were inconsistent (Philippat et al., 2012; Wolff et al., 2008). An inverse but non-significant association was found between TCS and birthweight among male, but not female infants in a U.S. study (Wolff et al., 2008). There were a few studies that examined the association between TCS and obesity (Lankester et al., 2013; Li et al., 2015). A recent study reported that urinary TCS level was associated with increased BMI in a U.S. adult population (Lankester et al., 2013).

In this study, we aim to explore whether maternal urinary TCS level is associated with GDM and birth outcomes in male and female infants in China.

2. Data and methods

2.1. Study population

This birth cohort study was initiated at the International Peace Maternity and Child Hospital (IPMCH), a large tertiary maternity hospital in Shanghai, China, in 2012. Pregnant women were recruited between 2012 and 2013 when they were hospitalized for childbirth. Eligibility criteria included: 1) having routine prenatal care at the study hospitals; 2) singleton pregnancy; 3) planned to reside in Shanghai during the 2-year follow-up period; and 4) willing to participate in this study and sign the consent form. After obtaining a written informed consent, trained nurses conducted a face-to-face maternal interview using a standardized questionnaire and collected spot urine samples. Given that 1/5 to 4/5 of the oral dose of TCS was excreted to urine during the first 4 days after exposure, and the plasma half-life of TCS was 21 h (Sandborgh-Englund et al., 2006), the urinary TCS concentration of the participants should represent their body burdens before hospital admission. The women usually delivered in the next day or two days after our investigation and sample collection. 71.6% of women delivered their infants by cesarean section (CS). After delivery, the study nurses reviewed maternal and infant medical records using a standardized abstraction form to obtain clinical data, including prenatal care, laboratory reports, pregnancy complications, labor and delivery course, and birth outcomes (infant sex, gestational age, birth weight, and birth length). All subjects gave an informed consent.

There were 680 eligible women who were enrolled. For this analysis, we excluded 60 enrolled women because they: did not collect urine sample (n = 38), had a medical complication (syphilitic) (n = 3), conceived by assisted reproductive technologies (ART) (n = 15), or had no urinary creatinine data (n = 1), urinary creatinine concentration < 5 mg/dL (n = 2) (Barbanel et al., 2002) or >300 mg/dL (n = 1) (Barr et al., 2005). This report included 620 women and their infants. 79 women had GDM. Power calculation was based on two-sample (GDM versus non-GDM) *t*-test. If we set significance level (alpha) = 0.05, to detect an effect size 0.35 (i.e. midway between small and medium), the power is 0.83.

This study was approved by the institutional review board of Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine and the International Peace Maternity and Child Hospital. All methods were performed in accordance with the relevant guidelines and regulations.

2.2. TCS exposure assessment

The urine samples were stored at −80 °C in polypropylene tubes until they were shipped on dry ice to the Xinhua Hospital, where they were stored at −80 °C before TCS analyses. TCS level was assayed with high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS) analytical method (Agilent 1290–6490, the United State) (Chen et al., 2012). Briefly, 4 mL urine sample was incubated with 2 mL of 1 mol/L ammonium acetate buffer solution (pH = 5.0) for hydrolyzation with 10 μL of β-glucuronidase/sulfatase (20,000 units/mL) at 37 °C overnight. Then the TCS was extracted and preconcentrated with solid phase extraction [500 mg/3 mL, Supelclean ENVI-18, USA]. After drying, the residue was dissolved in methanol. The solution was analyzed by LC-MS/MS. The limit of detection (LOD) was 0.1 ng/mL. The intra- and inter-day CV (coefficient of variation) for TCS were 1.4%–4.6%, and 3.0%–7.4% respectively. The solid phase extraction (SPE) recovery of TCS was 76.9%, and the accuracy (spike) recovery was 88.4%–110%, which indicated that the method is good and reliable. We prepared quality control (QC) samples from spiked pooled urine and analyzed QC samples along with standards, blanks and our urine samples. Creatinine concentrations of urine were measured with an automated chemistry analyzer (7100 Hitachi, Japan).

2.3. Outcomes

2.3.1. Main outcomes

2.3.1.1. Definition of GDM. The screening for and diagnosis of GDM followed the recommendation of International Association of Diabetes and Pregnancy Study Groups (IADPSG) (ADA, 2013). Specifically, GDM was defined if a woman had any of the following plasma glucose values: (1) Fasting: ≥5.1 mmol/L; (2) 1 h: ≥10.0 mmol/L; and (3) 2 h: ≥8.5 mmol/L in the 75-g oral glucose tolerance test (OGTT) which was performed at 24–28 weeks of gestation (ADA, 2013). All the diagnoses of GDM were also verified by the obstetricians.