Research paper

Bile acid metabolites in early pregnancy and risk of gestational diabetes in Chinese women: A nested case-control study

Jing Li [a], Xiaoxu Huo [a], Yun-Feng Cao [b,c], Sai-Nan Li [d], Zuo Du [d], Ping Shao [e], Junhong Leng [e], Cuiping Zhang [e], Xiao-Yu Sun [b,c], Ronald C.W. Ma [f], Zhong-Ze Fang [d,], XilinYang [a,]

[a] Department of Epidemiology and Biostatistics, School of Public Health, Tianjin Medical University, Tianjin, China
[b] Key Laboratory of Liaoning Tumor Clinical Metabolomics (KLLTCM), Jinzhou, Liaoning, China
[c] RSKT Biopharma Inc, Dalian, Liaoning, China
[d] Department of Toxicology, School of Public Health, Tianjin Medical University, Tianjin, China
[e] Tianjin Women and Children's Health Center, Tianjin, China
[f] Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China

a r t i c l e i n f o

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a b s t r a c t

fed mice are characterized by increased fasting glucose and a decreased bile acid pool size but improvement of insulin resistance after supple-

ethnicity, education attainment, habitual smoking before or during pregnancy, and alcohol consumption before or during pregnancy. Education attainment was classi ed into N12 or 12 years of schooling. Habitual smoking before or during pregnancy was de ned as continuously smoking one or more cigarettes per day for at least 6 months before pregnancy or smoking one or more cigarettes per day during pregnancy.

2.3. Metabolomics analysis of serum bile acids components

2.3.1. Sample pretreatment

Š 80 °C low temperature preservation of sample thawed in 4 °C. Quantitative weighing 50 µL sample in 1.5 mL EP, adding 2 µg/mL internal standard solution 10 µL, vortex 10 s, then 300 µL cold protein precipitation liquid (a methanol solution containing 0.1% ammonia) was added to the mixture, vortex 45 s, at 4 °C, the mixture was centrifuged for 10 min at a rotation speed of 16,000 g. After that, 200 µL of supernatant was transferred and concentrated to dry under nitrogen. Finally, the dried supernatant was dissolved with 50 µL methanol and 20 µL sample injection for LC/MS analysis. To ensure data quality, quality control (QC) samples were prepared by mixing all of the samples. During analysis of the sample sequence, one QC sample was run after every 30 injections.

2.3.2. LC-MS/MS analysis

Quanti cation of bile acids was performed according to previous studies with slight modi cation [19, 20]. Speci cally, an Eksigent ultral liquid chromatography 100 coupled with an AB 5600 Triple TOF system (AB SCIEX) was used to identify and quantify the bile acids components. A 2.1 × 100 mm XBridge Peptide BEH C18 column (waters) with a 4 × 2.0 mm guard column (phenomenex) was equipped to separate the different components. The separation was achieved under a column temperature of 40 °C using a controlled gradient of mobile phase A, which consisted of 0.1% (v/v) formic acid and 10 mM acetic acid amine in water, and mobile phase B, composed of 0.1% formic acid in 80% (v/v) methanol and 20% (v/v) acetonitrile, at a ow rate of 0.4 mL/min. The gradient ow was rst set at 35% (v/v) B for 0.5 min, linearly increased to 60% B during the next 2.5 min, linearly increased to 80% B during the next 7 min, linearly increased to 90% B during the next 6 min, linearly decreased to 35% B during3159 T(t)- 76(en025(s)]T)-268 TD9-10.4(a.3(r)-220(1(c

Inclusion of GUDCA and DCA in the traditional risk factor model significantly increased the AUC to 0.76 (95%CI: 0.71 . .0.80) (P b .0001) (Fig. 3).

4. Discussion

Our study has generated intricate ndings regarding the associations between individual bile acids and the risk of GDM. GUDCA and DCA had threshold effects for GDM and low GUDCA levels at 0.070 nmol/mL and low DCA levels at 0.280 nmol/mL were associated with markedly increased risks of GDM. Both associations were independent of traditional risk factors and the other bile acid.

Basic science research has unveiled important roles of bile acids in the regulation of glucose, energy metabolism, in ammation and various cellular processes [8]. Some small studies have also found associations of individual bile acids with T2DM. A study of 15 T2DM patients and 15 healthy controls showed that T2DM patients had elevated postpran-

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