

## **Risk for Recurrent Spontaneous Abortion in Relation to Phthalates Exposure in Taiwanese Reproductive-aged Women: A Case-Control Study**

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**Background** Recurrent spontaneous abortion (RSA) is the termination of pregnancies, usually before 20 weeks of gestation. Studies reported that phthalates might be involved in the pathogenesis of RSA, and that Taiwan's reproductive-aged women still expose to high levels of DEHP and DBP than other age groups after 2011 DEHP episode in Taiwan.

**Aim** We assessed the exposure and risk of phthalates in Taiwanese women with RSA.

**Methods** Between August 2013 and August 2017, we recruited 103 RSA patients and 76 controls from the obstetrics and gynecology department of a hospital in southern Taiwan. Urine samples were analyzed for 11 phthalate metabolites through liquid chromatography–tandem mass spectrometry; subsequently, principal component analysis (PCA) and agglomerative hierarchical clustering analysis were performed to determine the main sources of phthalate exposure. Finally, multivariate logistic regression was used to determine the RSA risk.

**Results** The creatinine-unadjusted (ng/mL) median levels of mono-n-butyl phthalate (MnBP), mono-iso-butyl phthalate (MiBP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), and mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP) were 27.2, 9.8, 11.4, and 12.9 ng/mL, respectively, in women with RSA and 13.1, 5.3, 8.1, and 9.5 ng/mL, respectively, in control women; furthermore,  $\Sigma$ DBP and  $\Sigma$ DEHP were 0.18 and 0.15 nmol/mL, respectively, in women with RSA and 0.10 and 0.12 nmol/mL, respectively, in control women. PCA revealed three primary components of phthalate exposure: diethyl phthalates (DEP), DBP, and DEHP. Plastic food container use and medication use were identified as the main phthalate exposure sources. After adjustment for potential confounding factors (creatinine, age, age at menarche, educational level, plastic food container use, and food preservation bag use), we observed significantly high adjusted odds ratios for RSA: 3.15 ( $p= 0.034$ ), 3.31 ( $p= 0.035$ ), and 2.57 ( $p= 0.074$ ) in the third tertile for MiBP,  $\Sigma$ DEHP, and  $\Sigma$ DBP, respectively.

**Conclusions** Our findings suggested that exposure to certain phthalates increases RSA risk in Taiwanese women possibly have an effect on the early development of implantation. Large and mechanistic studies are needed to elucidate the association.

Association between organochlorine pesticide levels in Taiwanese breast milk and their reproductive effects