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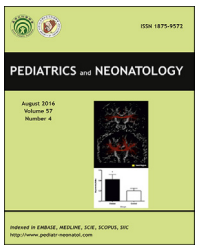

ORIGINAL ARTICLE

The Impacts of Cord Blood Cotinine and Glutathione-S-Transferase Gene Polymorphisms on Birth Outcome

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Key Words
cotinine;
environmental tobacco smoke;
glutathione S-transferase;
newborn;

Background: This study aimed to investigate the association between cord blood cotinine levels and birth outcome, and to determine whether fetal metabolic gene polymorphisms of glutathione-S-transferase (GST) modulate the effect of environmental tobacco smoke exposure during pregnancy.
Methods: This study included 328 maternal and neonatal pairs. Maternal and cord blood cotinine levels were measured using high performance liquid chromatography. The GST T1 (*GSTT1*) and GST M1 (*GSTM1*) polymorphisms were examined using the polymerase chain reaction

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premature birth;
small for gestational age

method. The birth outcomes included birth weight, length, and head circumference, and the risks of having low birth weight and being small for gestational age (SGA).
Results: Cord cotinine level had a dose-dependent impact on the reduction of birth weight, length, and head circumference in newborns. Elevation of cord blood cotinine concentration increased the rate of SGA and low birth weight. The neonates who had *GSTT1* or *GSTM1* polymorphism were associated with an increased risk of being SGA. A combination of the *GSTT1* and *GSTM1* null genotype exacerbated the effect of maternal environmental tobacco smoke exposure on SGA more than the presence of either genotype alone (odds ratio = 8.90, 95% confidence interval = 1.00–79.5).
Conclusion: Cord blood cotinine adversely affects birth outcomes. *GSTT1* and *GSTM1* null genotype may modify the effect of cord blood cotinine on birth outcomes.

1. Introduction

Although the percentage of smoking in the general population is declining, this trend has been slow among women of childbearing age.[1] The relationship between maternal smoking and adverse perinatal outcomes is well known with the prenatal risks of intrauterine growth retardation, low birth weight, and altered endocrine system.[2–4] Adverse neonatal outcomes include cleft palate/lip, behavioral problems, and sudden infant death.[5–7] In addition, maternal smoking is also associated with decreased lung function, increased risk of recurrent wheeze, and atopic dermatitis in childhood.[8–10]

Tobacco smoke contains more than 4000 compounds and most of them are metabolized in two steps that include the cytochrome P450 system and the detoxification process, by enzymes such as glutathione-S-transferase (GST) or uridine diphosphate-glucuronosyltransferase. GST catalyzes the conjugation of reduced glutathione with various compounds in order to inactivate and facilitate their excretion. Many classes of GST enzyme are known to exist in humans and each class has various subfamilies. The *GSTM1* and *GSTT1* genotypes have been well studied during recent years for their potential roles in the susceptibility to diseases under the influence of environmental factors.[11–13] Previous studies documented the relationship between enzyme polymorphisms and the degree of adverse effects of environmental smoking exposure.[14–16]

Several kinds of biomarkers are used for the prediction of neonatal outcomes among infants born to mothers smoking during pregnancy. Nicotine is the principal tobacco alkaloid, but it has a relatively short half-life.[17] Cotinine is the major metabolite of nicotine that has a longer half-life time than nicotine, and is the most sensitive biomarker for smoking and environmental tobacco smoke (ETS).[17] The level of cotinine in serum from mothers and neonatal cord blood can not only distinguish between those who engaged in smoking and nonsmoking during pregnancy, but it is also associated with poor outcome at birth. Previous studies showed that high ETS exposure in nonsmokers is associated with preterm labor,[18] and having a small-for-gestational-age baby.[19] However, few studies investigated the relation of fetus detoxification enzyme gene polymorphism with birth outcomes in maternal ETS during pregnancy.

The objectives of this study were to examine the relationship between cord blood cotinine concentrations, enzyme polymorphism, and birth outcomes, and also to assess the contributions of environmental tobacco exposure and genetic modification to birth outcomes.

2. Methods

2.1. Participants

This was a prospective cohort study that included maternal and neonatal pairs abstracted from the Taiwan Birth Panel Study project.[20] The project enrolled participants from one medical center, one local hospital, and two clinics between April 2004 and January 2005. Infants who were born at the participating hospitals and clinics without the presence of congenital anomalies and survived 24 hours of life were eligible for this study. The protocol was approved by the Institutional Review Board of National Taiwan Universal Hospital, Taipei, Taiwan.

Maternal and infant information was abstracted from the medical records. Maternal data included height, prepregnancy weight, total weight gain during pregnancy, complications in pregnancy and delivery, and medications used during pregnancy. Infant data included sex, gestational age, birth weight, birth length, birth head circumference, and Apgar scores. Low birth weight (LBW) was defined as a birth weight of a liveborn infant of less than 2500 g, and small for gestational age (SGA) was defined as having a birth weight less than the 10th percentile of national standard.

All participants were interviewed by trained research assistants using a structured questionnaire. Mothers completed the questionnaire within 3 days after delivery via self-report. The questionnaire contained demographics, a health checklist during pregnancy, history of active and passive smoking, environmental exposure, occupation history, maternal education, income level, and the use of alcohol, drug, and medication during pregnancy.

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