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The effect of maternal prenatal smoking and alcohol consumption on the placenta-to-birth weight ratio

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ABSTRACT

Background: Maternal influence on fetal growth is mediated through the placenta and this influence may have an implication for the offspring's long-term health. The placenta-to-birth weight ratio has been regarded as an indicator of placental function. However, few studies have examined the effect of maternal lifestyle exposures on the placenta-to-birth weight ratio. This study aims to examine the associations of maternal prenatal smoking and alcohol consumption with the placenta-to-birth weight ratio.
Methods: Data for 7945 term singletons, gestation≥37 weeks, were selected from the Tasmanian Infant Health Survey; a 1988–1995 Australian cohort study. Placenta and birth weight were extracted from birth notification records.
Results: Maternal smoking during pregnancy was strongly associated with a 6.77 g/kg higher (95% CI 4.83–8.71) placenta-to-birth weight ratio when compared to non-smoking mothers. Maternal prenatal smoking was associated with lower placental ($\beta = -15.37$ g; 95% CI −23.43 to −7.31) and birth weights ($\beta = -205.49$ g; 95% CI −232.91 to −178.08). Mothers who consumed alcohol during pregnancy had a lower placenta–to-birth weight ratio ($\beta = -2.07$ g/kg; 95% CI −4.01 to −0.12) than mothers who did not consume alcohol. The associations of maternal alcohol consumption during pregnancy with placental and birth weight did not reach statistical significance.
Discussion: Maternal prenatal smoking and alcohol consumption may influence fetal growth by either directly or indirectly altering the function of the placenta.
Conclusions: The alteration of the *in utero* environment induced by smoking and alcohol consumption appears to affect placental and fetal growth in differing ways. Further studies are needed to elucidate the mechanism.

1. Introduction

The health of a fetus is very much dependent on the environment in which it develops. More importantly, influences of the intrauterine environment during fetal growth may persist and may have an implication for the long-term health of the affected offspring. The developmental origins of adult disease hypothesis states that fetal under-nutrition at critical periods of *in utero* development results in adaptations in body structure and metabolism, leading to an increased risk of adult chronic diseases such as hypertension, diabetes, and cardiovascular disease [1].

The mother's influence on fetal growth is partly mediated through the placenta, a crucial organ for the exchange and transfer of substrates including nutrients and oxygen between mother and fetus [2]. However, the factors that determine placental size and function are still unclear. To date, epidemiological studies that have examined the effect of maternal factors on placenta have been almost entirely limited to maternal nutrition [3–5]. Although

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morphological studies suggest that smoking produces a decrease in size and vascularization of the placenta [6,7], few epidemiological studies have examined the associations of maternal prenatal smoking and alcohol consumption with placental growth, and such studies have been limited by a relatively small sample size [8,9] or the use of a dataset of a study conducted in the 1950's [10,11].

In this study, we used data from the Tasmanian Infant Health Survey (TIHS), a large cohort study, to examine the associations between maternal prenatal cigarette smoking and alcohol consumption, and placental weight and the placenta-to-birth weight ratio which is a widely used index for assessing placental function [12–14].

2. Methods

2.1. Participants

The TIHS was conducted between January 1988 and December 1995 with the primary objective of investigating the cause of Sudden Infant Death Syndrome (SIDS). Details of the study methods have been reported previously [15]. In summary, the study operated from six major obstetric hospitals in the state of Tasmania, Australia, where 93% of Tasmanian births occurred. Informed consent was obtained from the pregnant women. Infants were selected by a locally devised scoring system identifying infants at high risk of SIDS [16]. The sample of eligible infants represented one in five Tasmanian live-births.

The composite score for the predictive model included maternal age, neonatal gender, birth weight, season of birth (March–April, May–July, and August–February), duration of second stage of labor and intention to breast feed. Infants with a score over a specific cut-off point were eligible for the study. Data including sociodemographic, obstetric and perinatal information were collected by research assistants during a hospital interview when the neonate was about 4 days old. After excluding multiple pregnancies and infants born <37 weeks of gestation, the present analysis included 7945 mothers and offspring.

2.2. Study measures

2.2.1. Outcomes

Placental weight was measured wet after trimming the cord and without removing the membrane and attached blood clots. Placental status was assessed using visual inspection and classified as normal, incomplete, infarcted, post mature, clots on maternal side and other abnormality. As only around 1% placentas were classified as 'post mature' or 'clots on the maternal side', we combined them with 'other abnormality'.

2.2.2. Main exposures

Data on maternal prenatal cigarette smoking and alcohol consumption were collected during each trimester of pregnancy. Smoking was defined as: never smoked, smoked 1–10 cigarettes per day, smoked 11–20 cigarettes per day, and smoked 21+ cigarettes per day. Whilst alcohol consumption was defined as having consumed: no alcohol, 0–1 drinks per day, 2–3 drinks per day, 4–5 drinks per day, and 6+ drinks per day. As 97% of women who consumed alcohol during pregnancy reported drinking between 0 and 1 drinks per day, alcohol consumption was analyzed as a dichotomous variable (yes or no).

2.2.3. 3Covariates

The following variables were considered as covariates on the basis of possible associations with the outcomes and main exposures: components of the perinatal composite score used to determine eligibility of infants to participate in the TIHS, paternal age, maternal education, paternal education, household fortnightly income, maternal pre-pregnancy BMI (based on self-reported height and pre-pregnancy weight, kg/m^2), total pregnancy weight change (calculated as pregnancy weight prior delivery minus pre-pregnancy weight, kg), maternal passive smoking (whether or not lived with a smoker during pregnancy), parity, and gestational age of newborn (weeks).

2.3. Statistical analysis

We used descriptive statistics to report maternal and neonatal characteristics (mean and standard deviation for continuous variables, number (%) for categorical variables). We used multivariable linear regression models to examine the associations between main exposures and outcomes. We examined residuals graphically after fitting linear regression models to check for nonlinear associations and found evidence that linear models were adequate. We considered a range of potential covariates and used change-in-estimate criterion to detect covariates which could be included in the multivariable linear regression models. Finally, we involved components of the perinatal score (with the exception of birth weight) used to determine eligibility of the infant for inclusion in the study: maternal age, neonatal gender, season of birth (March–April, May–July, and August–February), duration of second stage of labor and intention to breast feed, and maternal education (as a proxy for maternal nutritional status and indicator of social economic status), parity, maternal pre-pregnancy BMI (kg/m^2), total pregnancy weight change (kg), maternal prenatal cigarette smoking (yes/no, except when smoking was the main exposure), maternal prenatal alcohol consumption (yes/no, except when alcohol consumption was the main exposure) and gestational age (weeks) in the multivariable linear regression models for all three outcomes (placenta-to-birth weight ratio, placental weight and birth weight). We tested for possible interactions between smoking and alcohol consumption during pregnancy with the composite eligibility score and found no indication of any interaction ($P > 0.40$). All statistical analyses were performed using Stata for Windows software (Version 11.1; StataCorp LP College Station, TX USA). We considered results for statistical analyses and interaction tests as significant if $P < 0.05$.

3. Results

Table 1 shows the characteristics of the study population. Birth weight data was available for all 7945 children whilst placental weight was available for 98.6%. Over half of the women (54%) had

Table 1
Maternal and neonatal characteristics of participants of the TIHS cohort included in the analysis.[a]

	$N = 7945$	Range
Maternal characteristics		
Age, years	23.25 ± 4.11	13.39 to 44.75
Education		
Primary school	1548 (20)	
High school	4934 (62)	
Completed secondary	1048 (13)	
Tertiary	358 (4.5)	
Parity		
First born	3628 (46)	
Second born	2659 (34)	
Third born	1152 (15)	
Forth born	362 (4.6)	
Fifth$^+$ born	133 (1.7)	
Any cigarette smoking during pregnancy (yes, no)	4282 (54)	
1st trimester		
Nil	3796 (48)	
1–10 cigarettes/day	1739 (22)	
11–20 cigarettes/day	1659 (21)	
21$^+$ cigarettes/day	666 (9.0)	
2nd trimester		
Nil	4047 (51)	
1–10 cigarettes/day	1609 (20)	
11–20 cigarettes/day	1597 (20)	
21$^+$ cigarettes/day	677 (9.0)	
3rd trimester		
Nil	4084 (51)	
1–10 cigarettes/day	1587 (20)	
11–20 cigarettes/day	1512 (19)	
21$^+$ cigarettes/day	748 (10)	
Any alcohol consumption during pregnancy (yes, no)	2662 (34)	
1st trimester	2286 (29)	
2nd trimester	2092 (26)	
3rd trimester	2054 (26)	
Pre-pregnancy BMI, kg/m^2	23.29 ± 4.80	13.87 to 52.16
Pregnancy weight change, kg	14.30 ± 6.59	−23 to 45
Neonatal characteristics		
Gender, male	5815 (73)	
Gestational age, weeks	39.64 ± 1.25	37 to 44
Birth weight, grams	3384.78 ± 603.20	1470 to 5845
Placental weight, grams	637.04 ± 154.16	175 to 1400
Placenta-to-birth weight ratio, g/kg	188.63 ± 33.88	69.07 to 392.67
Placental status		
Normal	4311 (55)	
Incomplete	429 (5.5)	
Infarction	138 (1.8)	
Other status (post mature, clots on maternal side and other abnormality)	2940 (38)	

[a] Characteristics reported as: mean ± standard deviation for continuous variables and number (%) for categorical variables.