

Impact of prenatal exposure to polycyclic aromatic hydrocarbons from maternal diet on birth outcomes: a birth cohort study in Korea

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Abstract

Objective: Polycyclic aromatic hydrocarbons (PAH) are common dietary exposures that cross the human placenta and are classified as a probable human carcinogen. The aim of the present study was to investigate the potential impact of exposure to PAH-containing meat consumed during pregnancy on birth outcomes.

Design: Prospective birth cohort study. Only non-smoking women with singleton pregnancies, who were free from chronic disease such as diabetes and hypertension, were included in the study. Maternal consumption of PAH-rich meat was estimated through FFQ. Multiple linear regression was used to assess factors related to higher intake and the association between dietary PAH and birth outcomes.

Setting: Republic of Korea, 2006–2011.

Subjects: Pregnant women (*n* 778) at 12–28 weeks of gestation enrolled in the Mothers and Children's Environmental Health (MOCEH) study.

Results: The multivariable regression model showed a significant reduction in birth weight associated with higher consumption level of foods rich in PAH, such as grilled or roasted meat, during pregnancy ($\beta = -17.48$ g, $P < 0.05$ for every 1 point higher in meat score). Further adjusting for biomarkers of airborne PAH did not alter this association. There was no evidence that higher consumption level of PAH-rich meat shortens the duration of gestation ($P = 0.561$). Regression models performed for birth length and head circumference produced negative effects that were not statistically significant.

Conclusions: Consumption of higher levels of barbecued, fried, roasted and smoked meats during pregnancy was associated with reduced birth weight. Dietary risk of PAH exposure in Korean women is of concern.

Keywords
Biomarker
Children
Polycyclic aromatic hydrocarbons
PAH-rich meat
Pregnancy
Birth weight

Polycyclic aromatic hydrocarbons (PAH), which are ubiquitous in the environment, are well known ecotoxicants and some of them are classified as a probable human carcinogen^(1,2). Automobile exhaust gas, industrial emissions and tobacco smoke were usually regarded as sources of human exposure to PAH^(3,4). However, more than a decade ago it was reported that PAH are formed in

a wide variety of foods during cooking at high temperature, especially when cooking meat over a combustion source^(5–7), and this is considered a major source of human exposure to PAH in non-occupationally exposed populations^(7–9).

PAH concentrations in food vary depending on different cooking methods and can contribute to the diet^(7,10) and to

the environment⁽¹¹⁾. Cooking foods at high temperature (grilling, roasting or frying) generates a large amount of PAH^(5,12,13). When meat is in direct contact with flame, PAH are formed due to pyrolysis of organic matter such as fat, protein, and carbohydrates, and become deposited on the outer surface of grilled or smoked meat^(14,15). Pyrolysis of fat has been shown to produce the greatest concentration of PAH⁽¹⁶⁾. Another possible mechanism of formation of PAH in grilled/smoked meat is the incomplete combustion of charcoal, which can generate PAH that are brought on to the surface of the meat⁽¹⁷⁾. The fat content of the meat and the proximity of the food to the heat source determine the PAH production in grilled or barbecued meat^(5,15). Other minor sources of exposure to PAH include house dust and contaminated soil and water^(18,19).

PAH are distributed to almost all internal organs after being absorbed into the human body, and most of them are rapidly metabolized and excreted in the urine. Therefore, it is possible to assess an individual's internal dose of PAH by measuring PAH and/or their metabolites in urine^(20,21). PAH metabolites in urine such as 1-hydroxypyrene (1-OHP) can be used as a biomarker of an individual exposure to airborne PAH^(20,22).

Several epidemiological and experimental studies have provided evidence of adverse effects of PAH on reproductive outcomes, including low birth weight and length, preterm birth, reduced head circumference at birth and lower scores on childhood tests of neurodevelopment^(23–26). Studies have reported that PAH compounds as well as others can exert their toxic effects on the mother and her fetus through the placenta^(27,28). The transplacental transfer of PAH to the fetus may have a significant impact on fetal development⁽²⁹⁾.

In view of the possible genotoxic and carcinogenic effects associated with PAH in grilled or smoked meat (PAH-rich meat)^(14,15,17), we investigated the association between prenatal dietary exposure due to consumption of PAH-rich meat and birth outcomes in the Republic of Korea. Only a few studies have investigated exposure to PAH from the consumption of grilled, smoked or roasted meats in pregnant women and have assessed its relationship with birth outcomes or lifestyle factors^(30,31). We assessed prenatal exposure to dietary PAH through maternal FFQ and associations between maternal dietary exposure to PAH and birth outcomes, hypothesizing that higher maternal intake of PAH-rich meat during pregnancy would be associated with reduced intra-uterine growth.

Materials and methods

Study population

The present study was conducted as part of the Mothers and Children's Environmental Health (MOCEH) study, which is a hospital- and community-based, multicentre,

prospective birth cohort study in the Republic of Korea. Details of the methods of the MOCEH study with specific eligibility criteria for the participation of mothers have been published earlier⁽³²⁾. The study sample comprised pregnant women at mid-pregnancy (i.e. 12–28 weeks of gestation) with a normal pregnancy (not-at-risk) who were enrolled during 2006–2011 in a community-based network of university hospitals, local clinics and community public health centres located in Seoul, Ulsan and Cheonan.

In total, 1825 pregnant women were recruited between 2006 and 2011. We excluded mothers reporting multiple births (n 30), diabetes or hypertension (n 71), missing birth length (n 384) or birth head circumference (n 336) or birth weight (n 12), missing data on meat consumption (n 154) or smoking (n 7), or missing data on urinary 2-naphthol (2-NAPH) and 1-OHP (n 53). Therefore, 778 mothers were included in the final analysis. We also compared the characteristics of the sample included in the study with those of the full sample and found no substantial differences, hence enhancing the overall confidence in the data available for the study.

Outcome variables

Information on medical history, psychosocial status, health behaviour, environmental exposure as well as socio-demographic characteristics was collected. The participants were followed up until delivery, and information on birth weight, birth length, head circumference, gestational age, parity and sex of the infant was obtained from medical records. The gestational age was estimated from the interval between the last menstrual period and the date of delivery and was corrected by ultrasonography measurement if there was a discordance of >10 d between both estimates. Small-for-gestational-age (SGA) children were those who weighed less than the 10th percentile for gestational age (mean birth weight for all SGA children: 2723 g).

Exposure assessment

Maternal diet

A well-trained dietitian administered a semi-quantitative FFQ to record usual dietary intake over a 1-year period prior to the interview. Maternal dietary intake was assessed during the first trimester of pregnancy using a 107-item FFQ. The FFQ method was previously validated in the Korean population^(33,34). The questionnaire had twenty-nine items on intake of processed meat, chicken and fish. The twenty-nine items also elicited information on the frequency of consumption of meats and fish products that involved grilling, roasting or smoking. The response categories for the frequency of consumption were divided into nine levels: '3 times daily', 'twice daily', 'once daily', '5 or 6 times weekly', '3 or 4 times weekly', 'once or twice weekly', '2 or 3 times monthly', 'once monthly' and 'never or seldom'. Information about portion sizes was collected

according to an appropriately defined unit (e.g. cup or bowl) and the sizes were classified into three categories: 'small', 'medium' and 'large'. For the present analysis we focused on commonly consumed meat and fish products and grouped these products into nine groups known to contain potentially high levels of PAH⁽³⁵⁾ based on similarities in the composition and processing of the meats in each group, specifically: 'barbecued beef', 'smoked beef', 'roasted/fried beef', 'barbecued pork', 'smoked pork', 'roasted/fried chicken', 'smoked chicken', 'roasted fish' and 'smoked fish'.

We created a PAH-rich meat score by giving 1 point for each of the meats and fish products that were consumed at least once in a week. The nine-item scale used a 1-week recall period. The food score was developed using the same procedures as used for creating an acrylamide food score for the assessment of maternal diet on birth outcomes⁽³⁶⁾. The responses on the nine items were summed to create the food score, with a minimum score of 0 indicating the lowest intake of PAH-rich meat and a maximum score of 9 indicating the highest intake. We excluded women with missing FFQ (n 154) in all dietary analyses.

Biomarkers

The urinary 1-OHP and 2-NAPH levels were used as biomarkers of personal exposure to airborne PAH, as also reported in a previous study⁽³⁷⁾. Maternal urine samples were collected in the morning and sent to a specialized laboratory for analysis. The 1-OHP and 2-NAPH levels were analysed by HPLC with fluorescence detection⁽³⁸⁾ and the levels that were measured during the first trimester of pregnancy were used for the present study. All data were adjusted to the urinary creatinine level to correct for urine volume. The biomarker data were expressed as median values or were natural log-transformed in the multiple regression models due to the skewed distribution of the data.

Potential confounders

The selection of confounders included in the adjusted models was based on a directed acyclic graph (see online supplementary material, Fig. S1)⁽³⁹⁾ and variables were chosen which seemed to have potential risk factors for the association of interest. Covariates examined in the analysis included the following: age at delivery (years), parity (≥ 1 *v.* 0); gestational age (continuous in completed weeks); weight gain in pregnancy (kg); maternal height (cm); maternal education (low, middle, high); sex of the infant (girl *v.* boy); high or low maternal consumption of fruits and vegetables during pregnancy (dichotomized by median intake); maternal intake of Fe (dichotomized by total median intake of Fe, dietary and supplemental, during pregnancy); and higher consumption of fish (>150 *v.* ≤ 150 g/d).

Statistical analysis

We used linear regression models for main birth outcomes assessed on a continuous scale (birth weight, length and head circumference at birth) and estimated β coefficients and 95% confidence intervals. Logarithmic binomial regression models were used to determine relative risks (RR) and 95% confidence intervals for SGA. We constructed several multivariable linear regression models, following the estimation of crude effects. Model 1 was adjusted for maternal age at delivery, education, maternal height, parity, gestational age, weight gain in pregnancy and sex of the infant. Model 2 was further adjusted for high or low maternal consumption of fruits and vegetables, maternal intake of Fe and higher consumption of fish. Models were robust to heteroscedasticity, and multicollinearity was not observed in our analysis as assessed by the variance inflation factor (value >10).

We used generalized additive models with cubic regression splines that were adjusted for gestational age, maternal height and maternal age to characterize the relationship between the consumption of PAH-rich meat and birth outcomes. These models were fitted in the statistical software R (www.r-project.org) using the *mgcv* package for generalized additive modelling. Other analyses were done in the statistical software package STATA 12. The significance level was set at $P \leq 0.05$.

Results

Sample characteristics

Table 1 describes the characteristics of the sample. The participating mothers were 30.5 years old and had a weight gain during pregnancy of 12.9 kg. About 52% of the pregnant women reported the consumption of barbecued or roasted or fried or smoked meats at least once in a week. Analysis of urinary 2-NAPH and 1-OHP from pregnant women included in the study showed the average concentration of 10.0 ng/g creatinine and 0.33 ng/g creatinine, respectively. The consumption of the meat and the biomarkers of PAH exposure were not correlated (Spearman's $r=0.005$, $P=0.838$ for the consumption of PAH-rich meat and 2-NAPH; Spearman's $r=-0.031$, $P=0.442$ for the consumption of the meat and 1-OHP), indicating that these biomarkers did not represent the recent consumption of barbecued, roasted, fried and smoked meats. The mean weight, length, head circumference at birth and gestational age of the infants under study was 3263.5 g, 50.5 cm, 34.0 cm and 38.8 weeks, respectively.

Regression results

The results of the regression analyses that examined the association between the consumption of PAH-rich meat and birth weight are summarized in Table 2. There was a

Table 1 Characteristics of the study sample and consumption of meat among pregnant women (*n* 778) at 12–28 weeks of gestation enrolled in the Mothers and Children's Environmental Health (MOCEH) study, Republic of Korea, 2006–2011

Sample characteristic	Total sample (<i>n</i> 778)	
	<i>n</i> or Mean	% or SD
Maternal age (years)		
Mean and SD	30.46	3.66
Missing (<i>n</i>)		102
Gestational age (weeks)		
Mean and SD	38.82	1.53
Missing (<i>n</i>)		1
Maternal height (cm)		
Mean and SD	161.30	4.55
Missing (<i>n</i>)		124
Maternal education, <i>n</i> and %		
Low	205	26.73
Middle	150	19.56
High	412	53.72
Missing (<i>n</i>)		11
Maternal weight gain in pregnancy (kg)		
Mean and SD	12.93	4.37
Missing (<i>n</i>)		123
Parity, <i>n</i> and %		
Nulliparous	401	55.93
Parous	316	44.07
Missing (<i>n</i>)		56
Sex of infant, <i>n</i> and %		
Boy	409	52.57
Girl	369	47.43
1-Hydroxypyrene (ng/g creatinine)		
Mean and SD	0.33	0.33
2-Naphthol (ng/g creatinine)		
Mean and SD	9.96	13.44
Length at birth (cm)		
Mean and SD	50.50	2.51
Birth weight (g)		
Mean and SD	3263.54	437.33
Head circumference at birth (cm)		
Mean and SD	33.97	1.52
Small for gestational age, <i>n</i> and %		
No	706	90.75
Yes	72	9.25
Vegetables (g/d)		
Mean and SD	262.18	163.08
Missing (<i>n</i>)		36
Fruits (g/d)		
Mean and SD	345.83	349.19
Missing (<i>n</i>)		36
Total Fe intake (mg/d)		
Mean and SD	25.90	8.18
Missing (<i>n</i>)		36
Fish consumption (g/d), <i>n</i> and %		
>150	70	9.43
≤150	672	90.57
Missing (<i>n</i>)		36
PAH-rich meat score, <i>n</i> and %		
0	375	48.20
1	138	17.74
2	142	18.25
3	57	7.33
4	34	4.37
5	15	1.93
6	10	1.29
7	4	0.51
8	2	0.26
9	1	0.13

PAH, polycyclic aromatic hydrocarbons.

Table 2 Estimated effect of consumption of polycyclic aromatic hydrocarbons (PAH)-rich meat on birth weight adjusted for socio-demographic, reproductive and lifestyle factors among pregnant women (*n* 778) at 12–28 weeks of gestation enrolled in the Mothers and Children's Environmental Health (MOCEH) study, Republic of Korea, 2006–2011

Characteristic	Model 1†		Model 2‡	
	β coefficient	95% CI	β coefficient	95% CI
PAH-rich meat consumption	-17.82	-34.63, -1.02**	-17.48	-34.32, -0.64**
Maternal weight gain in pregnancy	21.43	14.08, 28.79****	21.69	14.24, 29.15****
Gestational age	131.65	107.45, 155.83****	131.11	106.82, 155.39****
Maternal height	10.11	3.46, 16.77***	9.94	3.26, 16.62***
Maternal age	3.35	-5.09, 11.79	3.25	-5.19, 11.69
Maternal education				
Low		Reference		Reference
Middle	-73.59	-153.07, 5.89*	-80.13	-161.86, 1.60*
High	-11.78	-83.34, 59.79	-19.72	-93.01, 53.58
Parity (parous <i>v.</i> nulliparous)	139.13	77.44, 200.81****	138.08	76.01, 200.14****
Sex of infant (girl <i>v.</i> boy)	-119.69	-175.74, -63.65****	-121.92	-178.14, -65.70****
Fish consumption			6.56	-97.04, 110.17
Vegetables§			20.07	-41.08, 81.21
Fruits§			46.20	-12.52, 104.92
Fe intake§			-16.01	-77.65, 45.62
R^2	0.32		0.33	
<i>n</i>	607		607	

Statistically significant: * $P \leq 0.1$, ** $P \leq 0.05$, *** $P \leq 0.01$, **** $P \leq 0.001$.

†Adjusted for sex of the infant, parity, anthropometry of mother and gestational age.

‡Additionally adjusted for intakes of vegetables, fruits, Fe and fish. After further including biomarkers of PAH (1-hydroxypyrene and 2-naphthol; dichotomized by the median value of the distribution or natural log-transformed in separate models), the β and P values for dietary PAH were similar and significant. Moreover, the biomarkers were not significant predictors and were therefore not included in the models presented here.

§Dichotomized by the median value of the distribution.

significant negative association between higher consumption level of PAH-rich meat and birth weight. The mean birth weight was reduced by 17.82 (95% CI -35.63, -1.02) g with every 1 point higher in meat score after adjusting for sex of the infant, parity, anthropometry of mother and gestational age (model 1). After additionally adjusting for intakes of vegetables, fruits, Fe and fish (model 2), estimates remained significant (-17.48; 95% CI -34.32, -0.64 g; $P = 0.042$). Furthermore, inclusion of biomarkers of airborne PAH in model 2 did not substantially alter the estimated effect size or P value of dietary PAH on birth weight (-17.57; 95% CI -34.41, -0.72 g; $P = 0.041$; $n = 607$; biomarkers of airborne PAH dichotomized by their median values), indicating that prenatal airborne PAH is not a potential confounder of this association. Of the total variability in birth weight (32.4%) estimated from model 1, 0.1% could be attributable to the consumption of PAH-rich meat. The major variability in birth weight was explained by gestational age (21.0%), weight gain in pregnancy (7.1%), maternal height (2.6%) and sex of the infant (1.3%).

The results in Tables 3 and 4 demonstrate that coefficients on the meat scores for length and head circumference at birth were negative but not statistically significant. We further examined the combined association of dietary PAH and airborne PAH (dichotomized by the median value of the sum of two biomarkers of PAH) with birth length; the combined exposure produced a birth length deficit of 0.7 cm ($P = 0.005$). A test of the interaction term between dietary PAH and airborne PAH was not

significant ($P = 0.390$). A similar statistical approach for birth weight produced a birth weight deficit of 69 g for the combined exposure to dietary PAH and airborne PAH. The estimated effects were of borderline significance, and the test of the interaction term between dietary PAH and airborne PAH was not statistically significant ($P = 0.209$; see online supplementary material, Table S1).

A generalized additive model revealed that a 1-unit increase in the PAH-rich meat score was associated with a decrease in birth weight after adjustment for gestational age, maternal height and maternal age (Fig. 1). This also indicated that the pooled relationship between PAH-rich meat score and birth outcomes was approximately linear, indicating the appropriateness of linear regression models. In addition, the study revealed that birth outcomes (birth weight, length and head circumference) were significantly increased in association with pregnancy weight gain, gestational age, male sex of the infant, parity and maternal height. Moreover, a quadratic relationship between gestational age and birth outcomes was observed but additional adjustment for gestational age as a quadratic term (continuous completed weeks squared) gave nearly identical results (not shown).

In a separate analysis, the effect of consumption of PAH-rich meat on gestational age was tested. There was no evidence that higher intake level of meat shortened the duration of pregnancy ($\beta = 0.019$, $P = 0.561$, $n = 607$ in the model adjusted for sex of the infant, parity, anthropometry of the mother, and intakes of vegetables, fruits, Fe

Table 3 Estimated effect of consumption of polycyclic aromatic hydrocarbons (PAH)-rich meat on length at birth adjusted for socio-demographic, reproductive and lifestyle factors among pregnant women (*n* 778) at 12–28 weeks of gestation enrolled in the Mothers and Children’s Environmental Health (MOCEH) study, Republic of Korea, 2006–2011

Characteristic	Model 1†		Model 2‡	
	β coefficient	95% CI	β coefficient	95% CI
PAH-rich meat consumption	-0.07	-0.17, 0.03	-0.07	-0.17, 0.03
Maternal weight gain in pregnancy	0.06	0.02, 0.10***	0.06	0.02, 0.11***
Gestational age	0.72	0.54, 0.89****	0.71	0.53, 0.89****
Maternal height	0.06	0.02, 0.10***	0.05	0.02, 0.09***
Maternal age	0.01	-0.05, 0.06	0.004	-0.05, 0.06
Maternal education				
Low		Reference		Reference
Middle	-0.23	-0.72, 0.26	-0.24	-0.74, 0.26
High	0.22	-0.18, 0.63	0.13	-0.27, 0.54
Parity (parous v. nulliparous)	0.51	0.12, 0.89***	0.53	0.15, 0.91***
Sex of infant (girl v. boy)	-0.71	-1.06, -0.37****	-0.73	-1.07, -0.39****
Fish consumption			0.32	-0.31, 0.95
Vegetables§			0.26	-0.10, 0.63
Fruits§			0.30	-0.06, 0.65*
Fe intake§			0.06	-0.32, 0.44
R ²	0.24		0.25	
<i>n</i>	607		607	

Statistically significant: **P* ≤ 0.1, ***P* ≤ 0.05, ****P* ≤ 0.01, *****P* ≤ 0.001.

†Adjusted for sex of the infant, parity, anthropometry of mother and gestational age.

‡Additionally adjusted for intakes of vegetables, fruits, Fe and fish. After further including biomarkers of PAH (1-hydroxypyrene and 2-naphthol; dichotomized by the median value of the distribution or natural log-transformed in separate models), the β and *P* values for dietary PAH were not substantially changed and were therefore not included in the models presented here.

§Dichotomized by the median value of the distribution.

Table 4 Estimated effect of consumption of polycyclic aromatic hydrocarbons (PAH)-rich meat on head circumference adjusted for socio-demographic, reproductive and lifestyle factors among pregnant women (*n* 778) at 12–28 weeks of gestation enrolled in the Mothers and Children’s Environmental Health (MOCEH) study, Republic of Korea, 2006–2011

Characteristic	Model 1†		Model 2‡	
	β coefficient	95% CI	β coefficient	95% CI
PAH-rich meat consumption	-0.01	-0.08, 0.06	-0.01	-0.08, 0.06
Maternal weight gain in pregnancy	0.04	0.01, 0.06***	0.04	0.01, 0.06***
Gestational age	0.30	0.17, 0.43****	0.30	0.17, 0.42****
Maternal height	0.03	0.01, 0.06***	0.03	0.01, 0.05**
Maternal age	0.06	0.03, 0.09****	0.06	0.03, 0.09****
Maternal education				
Low		Reference		Reference
Middle	-0.28	-0.57, 0.02*	-0.32	-0.62, -0.02**
High	0.14	-0.12, 0.41	0.11	-0.16, 0.38
Parity (parous v. nulliparous)	0.34	0.11, 0.58***	0.34	0.10, 0.57***
Sex of infant (girl v. boy)	-0.55	-0.76, -0.33****	-0.55	-0.76, -0.33****
Fish consumption			-0.10	-0.46, 0.27
Vegetables§			-0.06	-0.30, 0.18
Fruits§			0.20	-0.03, 0.42*
Fe intake§			0.08	-0.16, 0.31
R ²	0.17		0.18	
<i>n</i>	607		607	

Statistically significant: **P* ≤ 0.1, ***P* ≤ 0.05, ****P* ≤ 0.01, *****P* ≤ 0.001.

†Adjusted for sex of the infant, parity, anthropometry of mother and gestational age.

‡Additionally adjusted for intakes of vegetables, fruits, Fe and fish. After further including biomarkers of PAH (1-hydroxypyrene and 2-naphthol; dichotomized by the median value of the distribution or natural log-transformed in separate models), the β and *P* values for dietary PAH were not substantially changed and were therefore not included in the models presented here.

§Dichotomized by the median value of the distribution.

and fish). Therefore, the observed deficit in birth weight and other birth outcomes was not mediated by shortening the gestation period. Furthermore, SGA was increased in association with increased consumption of PAH-rich

meat, but the association was of borderline significance when adjusted for gestational age, weight gain during pregnancy and parity (RR = 1.27; 95% CI 0.96, 1.68; *P* = 0.096; *n* 651).

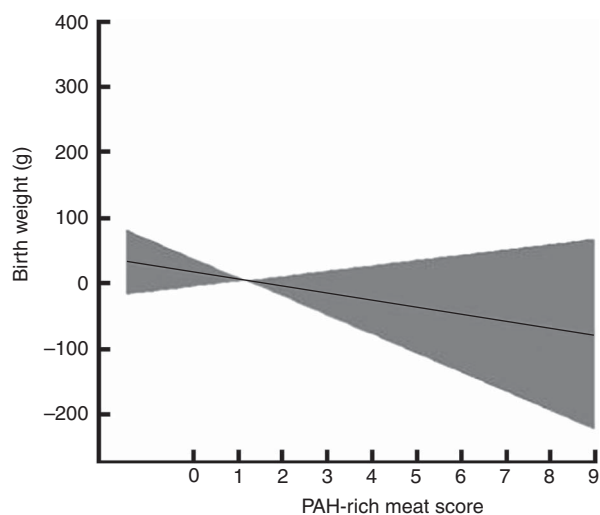


Fig. 1 Association of the polycyclic aromatic hydrocarbons (PAH)-rich meat score with birth weight among pregnant women (n 778) at 12–28 weeks of gestation enrolled in the Mothers and Children’s Environmental Health (MOCEH) study, Republic of Korea, 2006–2011. Generalized additive models with cubic regression spline for PAH-rich meat score adjusted for gestational age (completed weeks), mother’s height and mother’s age, showing the fitted smoothing spline (—) and the corresponding 95% confidence interval (■)

Discussion

The current study provides evidence that higher prenatal exposure to PAH through maternal consumption of PAH-rich meat during pregnancy is associated with reduced birth weight but not significantly associated with reduced birth length and head circumference. The higher consumption level of PAH-rich meat during pregnancy predicted a birth weight deficit of 17.5 g after controlling for sex of the infant, parity, anthropometry of the mother, gestational age, and maternal intakes of vegetables, fruits, Fe and fish. The relationship between prenatal dietary PAH and birth weight remained significant after controlling for biomarkers of airborne PAH. There was no significant interaction term between the exposure to dietary PAH and airborne PAH ($P = 0.209$), suggesting that the observed effects reflect the summarized exposure to both PAH sources rather than their synergistic effects. Furthermore, the shortening of gestational age was not mediated by the reduction in birth weight which was attributed to dietary PAH. Therefore, the duration of pregnancy was not associated with the exposures in question. In addition, there was a near significant association of SGA with an increased consumption of PAH-rich meat. Given these findings and previous evidence of possible adverse birth outcomes such as low birth weight and length, and poor neurodevelopment associated with PAH exposure during pregnancy^(25,26), the dietary contribution to PAH exposure in this population is of concern.

Effects of dietary PAH exposure on birth weight in this population were in agreement with findings from a recent study examining the possible impact of co-exposure to PAH-containing grilled meat consumed during pregnancy on birth outcomes in Poland⁽³¹⁾. The authors reported that the combined effect of exposure to both airborne and dietary sources of PAH amounted to a birth weight deficit of 214 g in the Polish population. However, in our study, airborne PAH did not confound the association between dietary PAH and birth outcomes. A separate model revealed that the combined effects of dietary PAH and airborne PAH (69 g) was lower than that reported in Poland. Such differences may be due to differences in the methods used to assess exposure to dietary intake or estimates of PAH concentrations. Nevertheless, our result of a mean birth weight deficit of 17.5 g with a 1-unit increase in the PAH-rich meat score is similar to the results obtained for the acrylamide food score⁽³⁶⁾. Earlier studies reported significant negative associations of maternal PAH exposure, which was estimated based on DNA adducts reflecting PAH exposure from all sources⁽⁴⁰⁾, or personal measure of atmospheric PAH exposure, with birth weight, birth length and SGA in populations from the USA^(25,29,41,42), Poland^(25,43) and the Czech Republic⁽⁴⁴⁾.

Although diet is recognized as the main source of human exposure to PAH in non-occupationally exposed individuals, there have been few data on the exposure to these compounds through maternal diet during pregnancy. One study in Spanish women found that elevated first-trimester dietary PAH, based on FFQ, was significantly associated with a birth weight deficit of 143 g (fourth *v.* first quartile)⁽⁴⁵⁾; similarly, a study in the same cohort described the associations between prenatal exposure to dietary PAH and fetal growth⁽⁴⁶⁾. A recent publication from a large Norwegian study demonstrated that higher prenatal exposure to dietary PAH was significantly associated with reduced birth weight⁽⁴⁷⁾. However, these studies used the consumption of a wide range of food items (meats, seafood, dairy products, cereals/potatoes, fruit, vegetables, eggs, legumes, beverages) as indicators of total dietary exposure to PAH and reported no association with birth weight when a limited number of food items (smoked, grilled or barbecued meats) were considered as indicators of dietary PAH⁽⁴⁷⁾.

Previous studies have reported that consumption of processed or cured meat and meat products is positively associated with the formation of PAH–DNA adducts^(48,49). It has been found that individuals who consumed barbecued food more than twice in the previous 2 weeks had fourfold increased risk of having elevated adducts level compared with individuals consuming the food two or fewer times⁽⁴¹⁾. Moreover, PAH–DNA adducts have been found in the placenta of women⁽⁵⁰⁾. This suggests that exposure to PAH-rich meat could affect the functions of the placental cells and consequently be a source of genotoxicity during fetal development⁽⁵¹⁾. The latter study

was not able to show the association between the consumption of PAH-rich meat in pregnancy and cord blood PAH-DNA adducts due to data limitation. However, DNA adducts formation is subject to a greater variability. The variability in results could be due to differences in metabolic phenotypes related to genetic polymorphisms⁽⁵²⁾ or plasma antioxidants may have modulated the effect of prenatal PAH exposure on PAH-DNA adducts in cord blood⁽⁵³⁾.

In addition to dietary intake of PAH, it is possible that biomarkers of airborne PAH were acting as a proxy marker for another dietary exposure or mix of other exposures such as environmental tobacco smoke that were responsible for the associations observed. Moreover, the consumption of meat might be a proxy indicator of some lifestyle factors^(54,55). However, adjusting for indicators of lifestyle factors such as intakes of fruits and vegetables, Fe and beverages, maternal characteristics, indicators of socio-economic status and environmental tobacco smoke (dichotomized based on a cut-off of 4.2 ng/g creatinine, obtained by receiver-operating characteristic curve analysis) did not substantially alter associations among the subset of the population with available data. Given the consistency of findings in different population subgroups and after adjustment for multiple potential confounders, it seems unlikely that prenatal exposure to tobacco smoke or other dietary compound(s) could fully explain the associations observed between PAH-rich meat and birth outcomes.

Findings of the present study are strengthened through statistical adjustment for multiple covariates at different levels including Fe, fruits and vegetables in the maternal diet. The findings are also largely consistent with theoretical expectations and the previous literature on this topic. Cases with missing data were excluded from our study. This may have had some effects on the findings because of a loss of information that may have affected the precision of the estimates. However, the potential bias in the study was decidedly low because the main characteristics for the full sample were almost identical to the characteristics of the sample that was available for the regression models. The exposure to PAH via food consumption was not assessed in the present study. However, the levels of PAH in food sources are considered to be consistent within the same area and exposure to PAH in most people could be similar⁽⁵⁶⁾. The lack of precise information on timing of the consumption of processed meat during pregnancy and the estimates of PAH dietary exposure from only an FFQ based on 1-week recall may be subject to recall bias. However, there did not appear to be any differential recall bias, as the dietary survey was carried out before the pregnancy outcome⁽⁵⁷⁾. Nevertheless, a well-trained dietary interviewer with standard protocol was used to minimize potential errors in assessing dietary intakes. Furthermore, the consumption of PAH-rich meat reported for a short period may not necessarily reflect dietary intake during the entire period of pregnancy. The questionnaire

on PAH-rich meat consumption in pregnant women in our study population has not yet been validated directly; however, a previous study has shown that use of a similar FFQ could produce acceptable reproducibility and modest validity of food consumption in Korean adults living in a metropolitan area⁽³⁴⁾.

Mechanisms underlying the effects of PAH on birth outcomes are not fully understood. The ability of PAH to readily damage DNA which may induce apoptosis, the anti-oestrogenic effects of PAH, and the binding of PAH to the human aryl hydrocarbon receptor to induce P450 enzymes or to receptors for placental growth factors that can result in decreased exchange of oxygen and nutrients, have been suggested to form the basis of some of PAH's toxic effects⁽⁴⁴⁾ and may contribute to the associations with birth outcomes in our study population. Further studies are warranted to explore the mechanisms underlying the action of antioxidants and prenatal PAH exposure on PAH-DNA adducts based on the precise time of consumption of processed meat and their implication on adverse pregnancy outcomes. Our findings have substantial public health implications because reduced birth weight is a risk factor for numerous adverse health effects early in life. In addition, it has also been associated with multiple adverse outcomes (reduced stature, increased incidence of CVD, type 2 diabetes mellitus and osteoporosis) later in life⁽⁵⁸⁾.

Conclusion

In conclusion, the present large, population-based, multicentre, prospective cohort study has provided epidemiological evidence of a significant association between prenatal exposure to dietary PAH and reduced birth weight. The results of the study suggest that dietary PAH exposure may also be an important source of additional risk of reduced intra-uterine growth among Korean women. The findings of the study can provide public health advice to pregnant women to reduce their dietary intake of foods that may contain high concentrations of PAH; however, further investigations are warranted to validate our findings.

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the MOCEH study and critically revised the manuscript. All authors read and approved the final manuscript. *Ethics of human subject participation*: The study protocol was approved by the institutional review board at Inha University, Incheon, Republic of Korea. Trained nurses were used to interview participants after getting a written informed consent from each woman who visited the community-based network of university hospitals, local clinics and community public health centres located in Seoul, Ulsan and Cheonan.

Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S1368980016000550>

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