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Exposure to air pollutants during the early weeks of pregnancy, and placenta praevia and placenta accreta in the western part of Japan

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ABSTRACT

Background: Placenta praevia is an obstetric complication involving placental implantation in the lower uterine segment. Given the suggested aetiology of placenta praevia, adverse biological effects of air pollutants, such as plasma viscosity increment, endothelial dysfunction, and systemic inflammation, have the potential to induce low implantation. We explored the association between exposure to air pollutants during the pregnancy period up to implantation, and placenta praevia, in pregnant Japanese women. The outcome also included placenta accreta, which often exists in combination with placenta praevia.

Methods: From the Japan Perinatal Registry Network database, we obtained data on 40,573 singleton pregnant women in western Japan (Kyushu-Okinawa Districts) between 2005 and 2010. We assigned pollutant concentrations (suspended particulate matter [SPM], ozone, nitrogen dioxide [NO_2], and sulphur dioxide [SO_2]), measured at the nearest monitoring station to the respective delivery hospital of each woman. A logistic regression model was used to adjust for several covariates.

Results: The odds ratios (ORs) of placenta praevia per 10 units increase were 1.12 (95% confidence interval (CI) = 1.01–1.23) for SPM over 0–4 weeks of gestation, and 1.08 (1.00–1.16) for ozone. The association between exposure to NO_2 and SO_2, and praevia, was in the direction of increased risk. SPM exposure during 0–4 weeks was associated with placenta accreta without praevia (OR = 1.33, 95% CI = 1.07–1.66). We found no association with exposure to air pollutants during 5–12 weeks and the second trimester.

Conclusions: Exposure to air pollutants through to implantation was positively associated with placenta praevia and accreta.

1. Introduction

The pathways linking ambient air pollution to adverse birth outcomes, such as preterm birth and low birth weight, are not fully understood. Recent studies reported that exposure to air pollutants was associated with obstetric complications, such as hypertensive disorders in pregnancy (Hu et al., 2014; Michikawa et al., 2015; Pedersen et al., 2014) that can result in prematurity and intrauterine growth restriction (Steegers et al., 2010). Therefore, hypertensive disorders are presumably an intermediate factor with regard to the association of air pollutants with adverse birth outcomes. In light of this, there is a possibility that obstetric complications may be key factors in the link between exposure to air pollutants and adverse birth outcomes.

Placenta praevia, wherein the placenta overlies or is proximate to the internal os of the uterus (Oyelese and Smulian, 2006), is one of the major causes of indicated preterm delivery, and is associated with maternal morbidity and mortality (Oyelese and Smulian, 2006; Vahanian et al., 2015). Although the aetiology of placenta praevia is still unclear, several factors, such as advanced maternal age, increased parity, smoking, prior caesarean delivery, prior placenta praevia (Oyelese and Smulian, 2006), are reported as potential risk factors for the condition. These factors are associated with ischaemia of the uterine endometrium and/or endometrial and myometrial damage, and are likely to lead to the placental implantation in the lower uterine segment (Faiz and Ananth, 2003). Adverse effects on the human body due to air pollution, including plasma viscosity increment, endothelial dysfunction, and systemic inflammation (Slama et al., 2008), may be a link to ischaemia of the endometrium and/or endometrial and myometrial damage, which means that exposure to air pollutants may disturb the implantation of the placenta in the upper uterus. Therefore, we hypothesised that exposure to air pollutants during the early weeks of pregnancy (i.e., the period up to implantation) is positively associated with the occurrence of placenta praevia.

Abbreviations: CI, confidence interval; NO_2, nitrogen dioxide; OR, odds ratio; PM, particulate matter; SPM, suspended particulate matter; SO_2, sulphur dioxide.

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The purpose of this study was to explore the association between exposure to air pollutants during the pregnancy period up to implantation, and placenta praevia in pregnant Japanese women. We also included placenta accreta, wherein the placenta adheres abnormally to the uterus (Oyelese and Smulian, 2006), as an outcome, because this condition often occurs in combination with placenta praevia (Garmi and Salim, 2012).

2. Materials and methods

2.1. Data source and participants

The Japan Perinatal Registry Network database includes all live births and stillbirths after 22 weeks of gestation, at cooperating hospitals throughout Japan (mainly university hospitals and local general hospitals). Anonymous information, such as maternal age, height, and weight, parity, gestational age (basically estimated by ultrasound findings during early pregnancy), smoking and alcohol consumption during pregnancy, infertility treatment, medical history, mode of delivery, and neonatal records, is regularly registered by attending physicians according to uniform coding specifications. Diagnoses of obstetric complications, such as placenta praevia and placenta accreta (our outcomes), are also registered on the database. This nationwide registry database covered 7.6% of the total live births and stillbirths in 2010. Details of the database, for which the Japan Society of Obstetrics and Gynaecology maintains and controls data quality, have been published elsewhere (Matsuda et al., 2011a, 2011b).

From the Japan Perinatal Registry Network database, we obtained data on 47,835 singleton births registered in 28 hospitals in the western part of Japan (Kyushu-Okinawa District), including 8 prefectures that are administrative areas of local government (Fukuoka, Saga, Nagasaki, Kumamoto, Oita, Miyazaki, Kagoshima, and Okinawa), between 1 January, 2005 and 31 December 2010. We focused on Kyushu-Okinawa District where there was the wide variation in air pollutant concentrations (Itano et al., 2013), to minimize the possibility of confounding derived from unknown local factors. Of the 47,835 women who delivered singleton births, we excluded those for whom pollution exposure data could not be assigned ($n = 1618$), and those without information on maternal age ($n = 3$). In addition, we excluded women who resided outside the prefecture of their delivery hospital ($n = 5641$), because we used air pollution data from the monitoring stations nearest the delivery hospitals. Thus, a total of 40,573 participants remained for final analyses.

Approval for the present study was obtained from the Institutional Review Boards of Kyushu University and the National Institute for Environmental Studies.

2.2. Environmental data

Exposure information, including suspended particulate matter [SPM], ozone, nitrogen dioxide [NO_2], and sulphur dioxide [SO_2], was collected from the Japan National Institute for Environmental Studies' atmospheric environment database. The daily mean concentrations of SPM, NO_2, and SO_2, as well as the maximum 8-h mean concentrations of ozone, were used. SPM, used as the basis for the Air Quality Standards in Japan (Japan Ministry of the Environment, 2009), is defined as airborne particles with a 100% cut-off level of 10 μm aerodynamic diameter. If SPM is defined in the same manner as fine particulate matter ($PM_{2.5}$), SPM is estimated as particles with a 50% cut-off level of 7 μm in aerodynamic diameter [PM_7]. Photochemical oxidants (i.e., mixtures of ozone and other secondary oxidants generated by a photochemical reaction) have been measured in Japan (Japan Ministry of the Environment, 2009); and as the concentrations of such oxidants are nearly equivalent to those of ozone (Japan Ministry of the Environment, 2010), we treated photochemical oxidants as ozone in this study.

Since the Japan Perinatal Registry Network database included only part of the participants' residential information (residence prefecture), we could not predict the respective concentrations of ambient air pollutants based on the specific residential addresses of the participants. Thus, we presumed that participants resided near their delivery hospitals, and assigned air pollution concentrations based on the nearest background monitoring station to the respective hospital of each participant. The median linear distance from each monitoring station to its respective hospital was 1.8 km (1.1 miles), and the distance was always <5 km except in the case of one hospital in Okinawa prefecture (13.6 km). The specific locations of the monitoring stations and hospitals have been previously provided (Michikawa et al., 2015).

Although our target exposure window was the first month of pregnancy (0–3 weeks of gestation) (Cha et al., 2012), namely the pregnancy period up to implantation, there is individual difference during this period. Therefore, we set an exposure window of 0–4 weeks of gestation in this study, and calculated the average concentrations of each pollutant over these 0–4 weeks, according to birth date and gestational age. In addition, to evaluate whether the pregnancy period up to implantation represented a sensitive exposure window for association with placenta praevia and accreta, we defined control exposure windows of 5–12 weeks of gestation (the late period of first trimester) and 13–28 weeks (the second trimester) (National Institute of Child Health and Human Development, 2013), and calculated the average concentrations of each pollutant during 5–12 weeks and 13–28 weeks.

2.3. Outcome

Placenta praevia and placenta accreta are independent obstetric complications. However, both conditions involve abnormal implantation of the placenta, and they often exist together (Garmi and Salim, 2012). Also, placenta accreta with placenta praevia is related to the occurrence of placenta praevia (Garmi and Salim, 2012; Oyelese and Smulian, 2006). In this study, we defined two outcomes: placenta praevia (partly including the cases of the coexistence with placenta accreta); and placenta accreta without placenta praevia.

2.4. Statistical analysis

Participants were categorised into quintiles based on the distribution of individual concentrations of each pollutant over 0–4 weeks of gestation, to check the dose-response association between exposure to air pollutants, and placenta praevia and accreta. In light of the

Table 1
Summary of average concentrations of each air pollutant during 0–4 weeks of gestation and Pearson's correlation coefficients among pollutants in the western part of Japan, 2005–2010.

Pollutant	*n*	Mean (SD)	Median (interquartile range)	Pearson's correlation coefficient			
				SPM (μg/m^3)	Ozone (ppb)[a]	NO_2 (ppb)	SO_2 (ppb)
SPM (μg/m^3)	40,461	27.5 (8.9)	27.3 (21.2–33.3)	1			
Ozone (ppb)[a]	36,820	41.3 (11.9)	39.9 (32.8–49.4)	0.17	1		
NO_2 (ppb)	36,807	11.9 (6.3)	11.8 (7.2–16.7)	0.45	−0.16	1	
SO_2 (ppb)	40,176	3.2 (1.6)	3.0 (2.0–4.2)	0.22	−0.09	0.40	1

NO_2 = nitrogen dioxide, SO_2 = sulphur dioxide, SD = standard deviation, SPM = suspended particulate matter.
[a] Daily maximum 8-h mean concentrations.