Environmental Research 142 (2015) 644–650

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

A register-based study of the association between air pollutants and hypertensive disorders in pregnancy among the Japanese population

Takehiro Michikawa [a,*], Seiichi Morokuma [b], Kotaro Fukushima [c], Kayo Ueda [a,d], Ayano Takeuchi [a,e], Kiyoko Kato [b], Hiroshi Nitta [a]

[a] Environmental Epidemiology Section, Center for Environmental Health Sciences, National Institute for Environmental Studies, Onogawa 16-2, Tsukuba, Ibaraki 305-8506, Japan
[b] Department of Obstetrics and Gynecology, Kyushu University Hospital, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan
[c] Department of Obstetrics, Fukuoka Children's Hospital, 5-1-1 Kashiiteriha, Higashi-ku, Fukuoka 813-0017, Japan
[d] Graduate School of Engineering, Kyoto University, Katsura, Sakyo-ku, Kyoto 615-8530, Japan
[e] Preventive Medicine and Public Health, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan

ARTICLE INFO

Article history:
Received 16 June 2015
Received in revised form
9 August 2015
Accepted 25 August 2015

Keywords:
Ozone
Hypertensive disorders in pregnancy
First trimester
Register-based
Japan

ABSTRACT

Background: Ambient air pollution is hypothesized to be a risk factor for hypertensive disorders in pregnancy, one of the major pregnancy complications. Past studies have reported the supporting evidence, however this mainly referred to the Western population, and results from trimester-specific analysis have been varied. In this study, we focused on exposure during the first trimester of pregnancy (placental development stage), and tested the hypothesis among the Japanese population.

Methods: We drew on data from the Japan Perinatal Registry Network database, and studied 36,620 singleton pregnant women without medical complications, in western Japan (Kyushu and Okinawa districts) between 2005 and 2010. In addition, data on ozone, suspended particulate matter (SPM), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) concentrations were obtained. The nearest monitoring station to the respective birthing hospital was used as a reference point for assigning average concentrations of each pollutant during the first trimester of pregnancy for each woman. The logistic regression model was applied to assess the association between quintiles of each pollutant and hypertensive disorders in pregnancy.

Results: Mean concentrations during the first trimester were 41.3 ppb for ozone, 27.4 μg/m^3 for SPM, 11.8 ppb for NO_2, and 3.2 ppb for SO_2. High exposure to ozone was associated with an increased risk of hypertensive disorders in pregnancy (for highest quintile vs. lowest: odds ratio=1.20, 95% confidence interval=1.01–1.42). With regard to SPM, NO_2 and SO_2, we did not obtain the results with constant directionality.

Conclusions: Ozone exposure during early pregnancy may be a risk factor for hypertensive disorders in pregnancy.

1. Introduction

Hypertensive disorders in pregnancy, including gestational hypertension, preeclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension (Brown et al., 2001), are complications of serious concern to obstetricians in clinical management of pregnancy, as they are prevalent conditions (5–10% of all pregnancies (Lo et al., 2013)) affecting pregnant women, and elevate the risk of maternal and fetus mortality and morbidity (Steegers et al., 2010). In addition, hypertensive disorders in pregnancy may affect not only the health of women during the gestational period, but also the future health of both mothers and their offspring. Earlier studies reported that preeclampsia was associated with increased risk of cardiovascular disease in the later life of pregnant women (Bellamy et al., 2007), and could affect the future health of their children born at term (Wu et al., 2009). Although past evidence provides insights into the importance of prevention of hypertensive disorders in pregnancy, there are few modifiable risk factors or preventive factors, from the point of view of public health. In light of this, the recent hypothesis that ambient air pollution is a risk factor for hypertensive disorders in pregnancy deserves attention (Hu et al., 2014; Pedersen et al., 2014).

Air pollution is an established risk factor for cardiovascular disease (Newby et al., 2015) and one biological explanation focuses

* Corresponding author. Fax. +81 29 850 2214.
E-mail address: tmichikawa@nies.go.jp (T. Michikawa).

http://dx.doi.org/10.1016/j.envres.2015.08.024
0013-9351/

on the pathway via systemic inflammation and oxidative stress by air pollutants (Newby et al., 2015). Experimental studies suggest that systemic inflammation and oxidative stress play a role in hypertensive disorders in pregnancy, in particular preeclampsia (James et al., 2010), though the etiology of hypertensive disorders in pregnancy is not fully understood. Based on such information, it is natural to suspect an association between air pollution and hypertensive disorders. Two systematic reviews have suggested the possibility that air pollution contributes to the occurrence of hypertensive disorders in pregnancy (Hu et al., 2014; Pedersen et al., 2014); however, there remains a dearth of publications on the association between air pollution and hypertensive disorders, and the results of trimester-specific analysis have been varied (Dadvand et al., 2013; Ibrahimou et al., 2014; Lee et al., 2013; Malmqvist et al., 2013; Mobasher et al., 2013; Olsson et al., 2013; Pereira et al., 2013; Wu et al., 2011; Xu et al., 2014). In addition, the majority of studies have been conducted on the Western population. One Japanese study used the mother's residential proximity to major roads, as a proxy marker of exposure to air pollutants, instead of actual concentrations of air pollutants (Yorifuji et al., 2015). Thus, further studies are needed to strengthen the epidemiological causal inference.

The present study investigated whether exposure to air pollutants was associated with the risk of hypertensive disorders in pregnancy among the Japanese population, focusing on exposure during the first trimester of pregnancy, because the pathogenesis of hypertensive disorders is considered to be established during the placentation period, over the first 12 weeks of pregnancy (James et al., 2010).

2. Methods

2.1. Data source and participants

The Japan Perinatal Registry Network database is managed by the Japan Society of Obstetrics and Gynecology. The details of this nationwide registry database have been published elsewhere (Matsuda et al., 2011a, 2011b). Briefly, the database consists of information on all live births and stillbirths after 22 gestational weeks, at cooperating hospitals, mainly university hospitals and local general hospitals. In 2010, 139 hospitals, which handled 7.6% of the total live and stillbirths in Japan, participated in the registration. At delivery, attending physicians regularly enter information such as maternal age, height and weight, parity, gestational age estimated by the last menstrual period, prenatal examination and ultrasound findings during early pregnancy, smoking and alcohol consumption during pregnancy, infertility treatment, medical history, obstetric complications, mode of delivery, and neonatal records, according to uniform coding specifications. Data quality control is performed by the perinatal committee of the Japan Society of Obstetrics and Gynecology. The database includes only anonymous data.

We applied for permission to use data from the Japan Perinatal Registry Network database and received data on the western part of Japan (i.e., Kyushu-Okinawa District), including eight prefectures (Fukuoka, Saga, Nagasaki, Kumamoto, Oita, Miyazaki, Kagoshima, and Okinawa). Although the database includes data on the whole of Japan, we focused on the western part of the country, to minimize the possibility of confounding due to unknown local factors, and because of the wide variation in air pollutant concentrations within the target district (Itano et al., 2013). Between 2005 and 2010, 47,835 singleton births were registered in 28 target hospitals. Of the 47,835 participants, we excluded 6032: in 948 cases the child was stillborn, 3595 had a history of heart disease and/or hypertension and/or diabetes mellitus, 1486 were not assigned any exposure data, and 3 had a lack of information on maternal age. In Japan, some pregnant women return to their parents and deliver at a hospital near their parents' home. Thus, to avoid exposure misclassification, we additionally excluded 5183 participants whose permanent residence was outside the prefecture of the hospital at which they delivered. These exclusions left, for final analysis, 36,620 women who had had singleton deliveries.

This study was approved by the Institutional Review Boards of Kyushu University and the National Institute for Environmental Studies.

2.2. Exposure data

We obtained data on ozone, suspended particulate matter [SPM], nitrogen dioxide [NO_2], and sulfur dioxide [SO_2] concentrations from the National Institute for Environmental Studies' atmospheric environment database. Ozone included secondary oxidants generated by photochemical reactions. According to the Japanese Air Quality Standards (Japan Ministory of the Environment, 2009), SPM is defined as airborne particles with a 100% cut-off level of 10 μm aerodynamic diameter, and estimated as particles with a 50% cut-off level of 7 μm in aerodynamic diameter [PM_7]; i.e., SPM particle size is between $PM_{2.5}$ (particulate matter < 2.5 μm in aerodynamic diameter) and PM_{10} (particulate matter < 10 μm in aerodynamic diameter). The hourly data in each background monitoring station was used to calculate maximum 8-h mean concentrations of ozone, and daily mean concentrations of SPM, NO_2, and SO_2. Ambient temperature data were obtained from the Japan Meteorological Agency.

Since the Japan Perinatal Registry Network database included only part of the participants' residential information (residence prefecture), we could not geocode the residential address of each participant. Thus, we assumed that participants resided near the hospitals where they gave birth, and assigned to each participant the data of the monitoring station nearest to the respective hospital (Supplementary figure). The linear distance between the respective hospitals and monitoring stations was less than 5 km (3.1 miles) (median, 1.8 km) except in the case of one hospital in Okinawa prefecture (13.6 km). Since our hypothesis aimed to explore the effects, on hypertensive disorders in pregnancy, of exposure to air pollutants during the first trimester of pregnancy (first 12 weeks of gestation), we calculated the average concentrations of each pollutant over the first trimester, based on birth date and gestational age. For example, a woman who delivered on January 20, 2009, at 40 weeks and 4 days, was assigned average concentrations from April 11 to July 10, 2008.

2.3. Hypertensive disorders in pregnancy

Information on diagnoses of hypertensive disorders in pregnancy by attending physicians was included in the Japan Perinatal Registry Network database. In the present study, we defined hypertensive disorders in pregnancy as gestational hypertension and preeclampsia. According to the criteria of the International Society for the Study of Hypertension in Pregnancy (Brown et al., 2001) and the guidelines of the Japan Society for the Study of Hypertension in Pregnancy (Watanabe et al., 2013), gestational hypertension is diagnosed as hypertension (systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg) after 20 weeks of gestation in women without hypertension before pregnancy. Preeclampsia is defined as hypertension with proteinuria (two or more dipstick readings of 3+ or greater, or a 24-h urine collection containing at least 300 mg of protein) (Watanabe et al., 2013). Although gestational hypertension and preeclampsia are different clinical conditions, we treated them as a combined outcome because the associations of air