The Japan Environment and Children’s Study (JECS) in Fukushima Prefecture: Pregnancy Outcome after the Great East Japan Earthquake

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Japan Environment and Children’s Study (JECS) is nationwide birth cohort study that was initiated in January 2011 to investigate the effect of environmental factors on children’s health. Soon after the JECS started, the Great East Japan Earthquake occurred on March 11, 2011, with subsequent nuclear accident at the Fukushima Daiichi Nuclear Power Plant, causing catastrophic damage in Fukushima Prefecture. After the disaster, JECS was relaunched to cover all areas in Fukushima Prefecture due to public concern. In this study, we used the results of individuals enrolled in JECS, who gave birth during 2011-2014 in Fukushima Prefecture, to elucidate pregnancy outcomes in Fukushima Prefecture. The study consisted of 12,804 maternal outcomes. We thus found that the prevalence rates of preterm birth < 37 weeks, low birth weight (LBW) < 2,500 g, and LBW < 1,500 g were 5.6%, 9.5%, and 0.8%, respectively; these rates are in accordance with the National Vital Statistics of 2014. The proportion of major anomaly among the newborns was 1.7%, the value of which was lower than other epidemiological studies. This study also found that severe obstetrics outcomes, such as hypertensive disorder of pregnancy and placental abruption, were most frequently seen among teenage mothers with low socioeconomic status. A prefecture-wide birth cohort study following a large-scale disaster may provide valuable information for obstetric care providers and residents to improve obstetric and perinatal care for pregnant women after a disaster.

Keywords: birth cohort study; natural disaster; nuclear power plant accident; obstetric outcome; teenage pregnancy

Introduction

Japan Environment and Children’s Study (JECS) is a nationwide and government-funded study started in January 2011 to investigate the effects of environmental factors on children’s health (Kawamoto et al. 2014). JECS is mainly structured with 15 regional centers and national center. In Fukushima, regional center for the JECS was established in Fukushima Medical University. At the beginning of JECS, pregnant women in Fukushima city, Minami Soma city, and Futaba County (Hirono Town, Naraha Town, Tomioka Town, Kawauchi Village, Okuma Town, Futaba Town, Namie Town, and Katsurao Village) were designed for the study. Soon after the start of JECS, Fukushima prefecture suffered from catastrophic natural disaster and subsequent nuclear accident at the Fukushima Daiichi Nuclear Power Plant (Fig. 1) (Fujimori et al. 2014). After the disaster, Fukushima regional center was relaunched to cover all areas in Fukushima prefecture, including 59 local municipalities (13 cities, 31 towns, and 15 villages) with 15 medical institutions in Fukushima Prefecture and 1 institution in Daigo Town in Ibaraki Prefecture on October 1, 2012. As a result, the target for the number of participants recruited was increased from 6,900 to 15,900 and Fukushima regional center made the largest contribution to recruit large number of participants for JECS (Hashimoto et al. 2017).

To our knowledge, a few birth cohort studies, which covered all the area within a single prefecture, have been performed in Japan (Fujimori et al. 2014; Kyozuka et al. 2016; Yasuda et al. 2017). The aim of this study is to provide maternal background and adverse obstetric outcome in a single prefecture using largest Japanese cohort study.
Materials and Methods

Study design
In this study, we used the data from JECS (Kawamoto et al. 2014). The recruitment criteria for participation in JECS were as follows: (1) Living in the study area at the time of recruitment, with expectation that they will continue to live in Japan in the future. (2) Expected delivery date falls within August 2011 to mid-2014 (Recruit started in January 2011 and continued for three years until March 2014). (3) Capable of participating in the study without difficulty (i.e., understanding Japanese language and being able to complete a self-administered questionnaire). The targeted recruitment rate was more than 50% for all the eligible mothers. Two following recruitment protocols were applied (1) recruitment at the first visit of pregnancy antenatal examination in cooperation obstetrics facilities and/or (2) recruitment at local government offices where the mothers received the Maternal and Child Health Handbook. Maternal and Child Health Handbook is given to all the expecting mother in Japan before receiving first municipal services for pregnancy, delivery, and childcare. Written informed consent were obtained from all the participants.

The JECS protocol was reviewed and approved by the Ministry of the Environment’s Institutional Review Board on Epidemiological Studies and by the Ethics Committees of all participating institutions (The National Center for Child Health and Development, Hokkaido University, Sapporo University, Asahikawa Medical College, Japanese Red Cross Hokkaido College of Nursing, Tohoku University, Fukushima Medical University, Chiba University, Yokohama City University, University of Yamanashi, Shinshu University, University of Toyama, Nagoya City University, Kyoto University, Doshisha University, Osaka University, Osaka Medical Center and Research Institution for Maternal and Child Health, Kyushu University, University of Occupational and Environmental Health, Kumamoto University, University of Miyazaki, and University of Ryukyu). The JECS was conducted in accordance with the Helsinki Declaration and other nationally valid regulations and guidelines. The present study was approved by the Institutional Review Board of Fukushima Medical University, which was responsible for the present study (IRB approval no. 1165).

Data collection
The current analysis used the dataset released in June 2016 (dataset: jecs-ag-20160424). In this dataset, we used three types of data: (1) M-T1, obtained from a self-reported questionnaire collected during their early trimester (the first questionnaire), which included questions regarding maternal medical background characteristics; (2) M-T2, obtained from a self-reported questionnaire collected during their second/third trimester (second questionnaire), which included partner lifestyle and socioeconomic status; and (3) Dr-0m, included obstetrics outcomes and maternal medical complications retrieved from medical records of each participants’ institution. The participants recruited at Fukushima Regional Center were included for this analysis.

Maternal medical background, socioeconomic status, and obstetric outcomes
Maternal medical background information was obtained from Dr-0m data (maternal age at the time of delivery, multiple pregnancy, BMI before pregnancy, primiparous or multiparous, diabetes mellitus (DM) before conception, and conception method); M-T1 data (age of menarche, maternal smoking status, and the Kessler 6-item psychological distress scale [K6]; and gynecological complication before pregnancy (myoma uteri, endometriosis, adenomyosis, uterine malformation, and ovarian tumor). BMI was calculated according to the World Health Organization standards (body weight [kg]/height [m]^2). We categorized subjects into three BMI groups as follows: < 18.5, 18.5-25.0, and ≥ 25.0 kg/m^2. The method of conception was categorized into natural or assisted reproductive technology (ART). We used the Japanese version of the K6 to screen for psychological distress in their first trimester. The K6 is a self-administered questionnaire that consists of six questions evaluating depressive state and anxiety on a scale from 0 (little to no depression or anxiety) to 4 (high levels of depression or anxiety). The K6 score is a continuous variable determined by the sum of six questions with a possible total score ranging from 0 to 24. A patient with a K6 score ≥ 13 was defined as having psychological stress (Kessler et al. 2002; Furukawa et al. 2008). Maternal participants were requested to provide information about their smoking status: “kept smoking during pregnancy,” “never smoked,” “quit smoking before pregnancy,” and “quit smoking during early pregnancy.” Maternal participants who chose “kept smoking during pregnancy” were classified into the smoking category, and others into non-smoking.

Socioeconomic status obtained from M-T2 data included annual household income, education state of the mother, education status of the partner, and smoking status of the partner. Annual household
income was categorized into four levels (< 2,000,000, 2,000,000-5,999,999, 6,000,000-9,999,999, and ≥ 10,000,000 JPY). The education status of the mother and the partner was categorized into four groups (< 10, 10-12, 13-16, and ≥ 17 years). The partners’ smoking status was classified similarly to the maternal smoking status.

Obstetric outcomes consisted of neonatal and maternal outcomes. Obstetric outcomes were obtained from Dr-0m data.

Neonatal outcomes included birth weight, low birth weight (LBW), weight of placenta, pH of the umbilical artery, sex, major anomaly of the newborn, and the mode of delivery. LBW was classified into two categories: LBW < 2,500 g and LBW < 1,500 g. The mode of delivery was categorized into vaginal or cesarean delivery. The major anomalies of the newborn observed are listed in Table 1 (International Clearing House for Birth Defects Monitoring Systems (ICBDMS Japan Center, https://www.icbdsrj.jp/data.html). The physical examination of newborns was conducted by the participants’ obstetricians, neonatologists, or pediatricians. If any major anomaly in the list was observed, they were defined as having a major anomaly of the newborn.

Maternal outcome included gestational age at birth, preterm birth (PTB), gestational diabetes mellitus (GDM), placenta previa, placenta accrete, placenta abruption, and hypertensive disorder of pregnancy (HDP). PTB was classified into two categories: PTB before 37 weeks and PTB before 34 weeks. HDP was further classified into early or late onset HDP. Early onset HDP was defined as onset of HDP < 30 gestational weeks and late onset HDP as onset after 30 gestational weeks.

Statistical analysis

The mothers were categorized into four age groups: < 20, 20-29, 30-39, and ≥ 40 years.

Maternal medical background, socioeconomic status, and obstetric outcomes were summarized according to the maternal age groups. Some obstetrical outcomes data that were retrieved from Japanese Vital Statistics or epidemiological studies conducted around the year 2011 were included in present analysis (Fujimori et al. 2014; Morikawa et al. 2014; Japanese Ministry of Health, Labour and Welfare 2015) (ICBDMS Japan Center). SPSS version 21 (IBM Corp., Armonk, NY) was used for all descriptive analysis.

Result

In the present analysis, the study data from mothers consisted of 11,921 maternal medical background data, 10,942 socioeconomic background data, 11,139 neonatal outcome data, and 12,804 maternal outcome data. The mean gestational age when M-T1 was conducted was 11.6 (1.1) weeks.

Table 2 shows the maternal medical background characteristics, overall and by age groups. The percentage of mothers who kept smoking during pregnancy was 4.0%, but it was highest in the youngest age group (9.8%). The percentage of mothers with DM was highest in those over 40 (2.3%) years of age. The prevalence of gynecological complications, such as endometriosis, adenomyosis, myoma uteri, uterine malformation, and ovarian tumor, increased with maternal age. The percentage of mothers with K6 score ≥ 13 at first trimester was highest among the younger age group.

Table 3 shows the socioeconomic characteristics by maternal age groups. While low annual household income (< 2,000,000 JPY) was more frequently seen in the youngest age group (26.5%), high annual household income (> 10,000,000 JPY) was more frequently seen in the oldest age group (9.0%). Similar to the mothers of the youngest age group, the higher percentage of partners of those < 20 years kept smoking during pregnancy.

Table 4 shows the number and percentage of neonatal outcomes by maternal age groups. Overall, the percentages of LBW < 2,500 g and < 1,500 g were 9.0% and 0.7%, respectively; these complications were more frequent among those aged over 40 years (11.0% and 1.0%, respectively). The proportion of major anomaly of the newborn

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<th>Major anomalies in newborns</th>
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was 1.7%. This percentage was highest among those aged over 40 years (3.2%).

Table 5 shows the number and percentage of maternal outcomes by maternal age groups. The percentages of PTB < 37 weeks and < 34 weeks were 5.5% and 1.7%, respectively. Similar to the prevalence of LBW, these complications were more frequently seen in those aged over 40 years (6.6% and 2.8%, respectively). The percentage of GDM (1.9%) was highest in those aged over 40 years (4.8%). Overall, the prevalence of placenta previa, abrupton, and accreta were 0.4% (49/12,804), 0.6% (75/12,804), and 0.2% (28/12,804), respectively. While placenta previa was most frequently seen in those aged over 40 years (1.1%), placenta abrupton was more frequent in those aged < 20 years (1.6%). HDP was shown in 318 cases (2.5%): 0.3% early and 2.1% late onset HDP. The prevalence of early and late
Early onset HDP was highest among those aged < 20 years (0.8% and 3.9%, respectively).

**Discussion**

The aim of this study was to describe both the baseline maternal background characteristics and the adverse obstetric outcomes in a single prefecture after the natural disaster. The present study indicated that the obstetric outcomes in Fukushima Prefecture after the disaster were compatible with those from the national survey conducted around the disaster period. Our study also found valuable information about teenage pregnancy indicating that young mothers tend to face socioeconomic disadvantages such as low annual household income, low maternal and paternal education, psychological stress (indicated by K6 score), and both maternal and partner smoking status during pregnancy, resulting in severe adverse obstetric complications such as placenta abruption or HDP (both early and late onset). This study also determined the prevalence of previously unknown gynecological complications. For example, a fourth (100/427) of women over 40 years developed myoma uteri.

A previous study with the nationwide Japan Perinatal Registry network medical record database, managed by the Japan Society of Obstetrics and Gynecology, reported that obstetric complications such as PTB < 37 weeks, placenta previa, placenta abruption, and HDP increased with maternal age (Matsuda et al. 2011). By contrast, our results suggest that obstetric complications such as placenta abruption and HDP (both early and late onset) are most frequent...
among mothers aged < 20 years, which is not consistent with the earlier report (Matsuda et al. 2011). This discordance might have resulted from the diagnostic criteria of placenta abruption or HDP as well as differences in population data sample. Socioeconomic risk factors more prevalent in teenage pregnancy were poverty, low educational level, inadequate prenatal care, and unmarried status (Bukulmez and Deren 2000; Gortzak-Uzan et al. 2001; Chen et al. 2007). Sufficient perinatal care for teenage pregnancy is said to improve perinatal outcomes (Bukulmez and Deren 2000). Our study showed high prevalence in smoking status, and psychological stress when screened using the K6 score. Accordingly, advise, for smoking cessation or counseling and follow-up, targeting teenage pregnancies might be one of the important perinatal care, to improve obstetric outcome in the entire prefecture.

Shortly after the start of JECS, Fukushima Prefecture suffered from an unprecedented natural disaster with subsequent nuclear power plant accident in March 2011. Natural disaster and nuclear power plant accident have reportedly shown potential influence on a range of reproductive and birth outcomes (Goldhaber et al. 1983; Xiong et al. 2008; Tan et al. 2009). Immediately after the disaster, Fukushima unit center received the request from pregnant women and medical institutions, for research to be conducted across the entire Fukushima Prefecture (Hashimoto et al. 2017). The Fukushima Health Management Survey (FHMS) is another study including geographical and birth data information that surveyed for pregnancy outcomes, to provide valuable data in the investigation of the health effect of low dose radiation and disaster related stress (Yasumura et al. 2012). In the survey, Fujimori et al. (2014) reported 238 congenital malformations in 8,436 births (2.7%) in the first year after the disaster, which was similar to the recent average in Japan (2.4%) (ICBDMS Japan Center). Contrary to FMFS which was conducted around almost the same period as JECS, the present study indicated a lower prevalence of major anomalies (1.7%, 192 cases/11,139 participants). Interpretation of newborn abnormality prevalence in both FMFS and JECS must be interpreted with caution. Obstetrics outcomes of JECS were retrieved from medical records of each institution, while outcomes of FMFS relied entirely on self-reported questionnaires that needed to be returned. Therefore, overestimation of the actual incidence of negative outcomes may exist if there was an overrepresentation of women who were affected by the disaster (Kyozuka et al. 2016).

There are several strengths to the present study. JECS is the first large nationwide population-based study in Japan combining medical records and biological samples managed by the Japanese government with meticulous attention to data precision. JECS also included various types of evaluation with unknown items for each pregnant woman such as, gynecological complications, age of menarche, and the K6 score. Furthermore, the present study is prospective study targeted pregnant mothers in a single prefecture, with less-selection bias.

Our study also has several limitations. First, almost all maternal background characteristics and socioeconomic status relied on a self-reported questionnaire. Therefore, we could not precisely determine the ART method or the types of uterine anomalies. However, because some maternal background characteristics and obstetric outcomes obtained from Dr-0m data were based on medical records collected by physicians, midwives, nurses, and trained research coordinators; these were more likely to be relatively accurate. Second, Khalil et al. (2013) reported that maternal ethnicity was related to adverse pregnancy outcomes; however, according to the JECS recruitment protocols, almost all participants in our study were restricted to Japanese women. Therefore, our results did not consider maternal ethnicity, and the findings may not be applicable to other ethnicities. Third, we could not obtain information on either the geographical area or the delivery date from the present JECS dataset because of the need for privacy and identity protection; namely, the present study could not analyze perinatal outcomes based on its relationships with the distance from the nuclear accident site or chronological factors. Geographical or birth data information may provide us with valuable information concerning perinatal outcomes after the disaster this therefore remains a challenge in the future. For both obstetric care providers and residents in Fukushima Prefecture, the obstetric outcomes across entire Fukushima Prefecture are of public health concerns.

In conclusion, the large-scale birth cohort study, which targeted entire Fukushima Prefecture, has provided valuable information concerning the unknown prevalence of maternal background characteristics and gynecological or obstetric complications. The present study has also provided the information to improve obstetric and perinatal care for pregnant women after a disaster.

Acknowledgments

The Japan Environment and Children’s Study was funded by the Ministry of the Environment Japan. The funding source had not involvement in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

We would like to thank all the participants in the study, as well as the cooperating medical institutions and government agencies, and staffs of Fukushima regional center of JECS. The list of the cooperating medical institutions is given below. None of these projects have any conflicts of interest to declare.

Kenpoku area: Fukushima Red Cross Hospital, Meiji Hospital, Ichikawa Clinic, Sasaya Obstetrics and Gynecology Clinic, Honda Obstetrics and Gynecology Clinic, Saiseikai Fukushima General Hospital, Ohara General Hospital, Fukushima Medical University Hospital, Okawa Lady’s Clinic, Kanno Obstetrics and Gynecology Clinic, Saint Clinic, Social insurance Nihonmatsu Hospital, Watanabe Clinic, Tani Hospital

Kencho area: Tanaka Lady’s Clinic, Okazaki Obstetrics and Gynecology Clinic, Jusendo General Hospital, Tsukahara Obstetrics, Gynecology, Internal medicine, and Surgery Clinic, Total Health Clinic, Furukawa Obstetrics and Gynecology
Pregnancy Outcome in Fukushima


