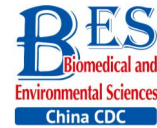# Letter to the Editor

Demographic Characteristics and Environmental Risk Factors Exposure of Birth Defects in Pregnant Women: A Population-based Study[*]

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Worldwide, the incidence of birth defects in low-income countries is 6.42%, while in middle-income and high-income countries it is 5.57% and 4.72%, respectively; approximately 303,000 newborns die from birth defects each year. In China, the incidence of birth defects is about 5.6%, and around 8.14 million people have congenital disabilities, accounting for 9.6% of total disabled people[1]. Birth defect remains a major clinical and public health challenge because of its high fatality rate and protracted and severe sequela.

Due to the complicated pathogenesis of diseases, many modifiable environmental risk factors related to birth defects have been identified, including heavy metals, solvents, pesticides, maternal illnesses, and maternal smoking, among others[2-4]. During early pregnancy, environmental risk factors can selectively act on the fetus tissues and organs that are in an active stage of development and differentiation, resulting in abnormalities in their morphology or function. Till date, more attention has been paid to the association and possible functioning of environmental risk factors leading to birth defects. However, the distribution of pregnant women exposed to environmental risk factors remains a major concern. There is still a lack of research with large sample sizes concerning exposure to environmental risk factors related to birth defects among pregnant women with different demographic characteristics. Therefore, we conducted this study to explore the association between demographic characteristics and exposure to environmental risk factors, which may help to identify populations at risk for birth defects and provide more effective and targeted prevention strategies for birth defects in China.

The study population included pregnant women who received prenatal care at medical institutions in Liuyang, Hunan, China between June 2013 and November 2014. Stratified random sampling was performed in this study. According to the urban-rural ratio, population density, and fertility levels, two streets and 11 towns were randomly selected in Liuyang city (four streets and 33 towns in total). Finally, all pregnant women who met the inclusion criteria were enrolled in this study in the chosen street or town. The inclusion criteria were the following: a) 16-20 gestational weeks; b) local resident for more than six months; and c) willing to participate in the survey. Pregnant women with severe physical symptoms and mental disorders who were unable to complete the survey were excluded. All participants provided written informed consent.

A face-to-face questionnaire survey was conducted with participants in order to gather information about their demographic characteristics and exposure to environmental risk factors, starting from three months before conception to the first trimester of pregnancy. The questionnaire was divided into two parts: part 1, demographic characteristics; and part 2, genetic risk factors and environmental risk factors (25 variables from four categories: physical and chemical risk factors, behavioral and lifestyle risk factors, disease and drug risk factors, and adverse reproductive history) (Supplementary Table S1, available in www.besjournal.com). The questionnaire was designed by experts from the research team and adjusted based on a pilot study.

The definition of each variable was provided to participants, for example: 1) education level was

classified into three categories: primary school and below, secondary school, and tertiary/high school; 2) X-rays contact: exposure to X-rays more than once a month or more than three times, or a large dose of contact; 3) passive smoking: no-smokers inhale smoke exhaled by smokers at least one day (> 15 min) in a week; 4) chronic diseases: history of doctor-diagnosed chronic diseases three months before conception, such as diabetes and hypertension, among others; 5) abortion: history of at least one abortion before this pregnancy; 6) maternal family history of birth defects: history of birth defects among relatives of maternal families within three generations; 7) exposure rate: proportion of pregnant women exposed to risk factors within the total number of pregnant women.

Standardized training was provided for all the researchers to ensure the quality of the interview. This study used dual data entry, and logical checks were performed during data entry. Data were analyzed using SPSS statistical software, version 18.0 (USA). Descriptive statistics were summarized using percentages, means, and standard deviations (SD), where appropriate. Separate logistic regression models were used to assess the association between demographic characteristics and exposure to every environmental risk factor. The significance level was determined at $\alpha = 0.05$.

Initially, a total of 10,475 pregnant women were surveyed; 312 of these women (3.0%) were excluded because of missing data (> 20%). Data from 10,163 pregnant women were further analyzed, and their demographic characteristics are shown in Supplementary Table S2, available in www.besjournal.com. In this study, the exposure rate to environmental risk factors was 94.0% and 1.8% concerning genetic risk factors. Within the environmental risk factors group, the highest exposure rate was observed in behavioral and lifestyle risk factors (88.7%), followed by adverse reproductive history (34.8%), physical and chemical risk factors (25.8%), and disease and drug risk factors (24.2%). Further, within these four categories, the most common risk factors found were the use of microwave ovens or induction cookers (9.5%), pickled or smoked food intake (55.9%), respiratory infection (17.5%), and abortion history (32.1%). Only 5.9% of pregnant women had not been exposed to any risk factors, as summarized in Supplementary Tables S3 and S4, available in www.besjournal.com.

As seen in Tables 1, 2, and 3, results from logistic regression analysis showed that youngest pregnant women had higher odds of renovating their house (OR = 2.75), using cosmetics (OR = 1.73), dyeing or perming hair (OR = 1.64), and were less likely to have an adverse reproductive history (OR = 0.25). Pregnant women with lower educational levels had increased risk of exposure to noise (OR = 1.91), toxic and hazardous substances (OR = 3.28), and fireworks production-related toxic substances (OR = 13.74), as well as an adverse reproductive history (OR = 1.73). Farmers and housewives had a lower risk of respiratory infections (OR = 0.50; OR = 0.49) and exposure to microwave ovens or induction cookers (OR = 0.60; OR = 0.65). Factory workers had higher exposure risk of fireworks production-related toxic substances (OR = 4.77). Women who were company employees or self-employed had higher exposure risk of cosmetics (OR = 1.41) and lower exposure risk of respiratory infections (OR = 0.56), as well as less risk of labor induction (OR = 0.37). On the other hand, rural pregnant women had higher risk of exposure to fireworks production-related toxic substances (OR = 2.11), environmental pollution (OR = 1.80), passive smoking (OR = 1.46), disease and drug risk factors (OR = 1.35), and lower risk of exposure to microwave ovens or induction cookers (OR = 0.62), and housing renovations (OR = 0.71). Pregnant women with lower income had a lower risk of exposure to cosmetics (OR = 0.76), pickled and smoked food (OR = 0.72), and passive smoking (OR = 0.75).

Previous research has shown that around 25% of birth defects are caused by genetic factors, and around 10% are due to environmental factors, while the remaining 65% birth defects may be caused by the combined effect of genetic and environmental factors or other unknown reasons. In this study, we found that the rate of exposure to environmental risk factors was much higher than that of genetic risk factors, which is in agreement with Zhang's[5] findings. Because environmental risk factors, which are different from genetic risk factors, can be controlled through interventions, we should monitor the exposure to environmental risk factors among pregnant women, and health education to reduce or avoid exposure to environmental risk factors should be prioritized.

In this study, we found that younger pregnant women had a greater probability of using cosmetics and dyeing or perming hair, which may be related to their concern regarding beauty and fashion. On the

Table 1. Association between Demographic Characteristics and Exposure to Physical and Chemical Risk Factors

Demographic Characteristics	Physical and Chemical Risk Factors[†]	Noise Pollution	Microwave Oven or Induction Cooker Use	Toxic and Hazardous Substances	Fireworks Production Related Toxic Substances	Housing Renovations	Environmental Pollution
Age (years)							
18-24	1.02 (0.84-1.25)	1.22 (0.86-1.74)	0.87 (0.64-1.17)	1.18 (0.65-2.16)	0.61 (0.44-0.84)**	2.75 (1.61-4.69)**	0.80 (0.47-1.38)
25-29	0.91 (0.74-1.11)	1.18 (0.83-1.67)	1.00 (0.74-1.35)	0.96 (0.53-1.75)	0.53 (0.39-0.74)**	1.43 (0.84-2.45)	0.60 (0.35-1.03)
30-34	1.00 (0.81-1.24)	1.01 (0.69-1.49)	0.84 (0.60-1.16)	1.23 (0.65-2.32)	0.95 (0.68-1.32)	1.27 (0.71-2.27)	0.82 (0.46-1.48)
35-47	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Educational level							
Below primary/primary	1.70 (1.23-2.33)**	1.91 (1.16-3.12)*	0.87 (0.49-1.53)	3.28 (1.32-8.14)*	13.74 (6.90-27.34)**	0.59 (0.25-1.40)	1.14 (0.47-2.74)
Secondary	1.15 (0.99-1.32)	1.13 (0.90-1.43)	1.10 (0.90-1.34)	2.15 (1.24-3.71)**	4.25 (2.34-7.74)**	0.82 (0.64-1.06)	0.84 (0.56-1.27)
Tertiary/higher	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Maternal occupation							
Farmer	0.87 (0.63-1.19)	0.58 (0.35-0.94)*	0.60 (0.39-0.92)*	1.06 (0.30-3.76)	2.41 (0.57-10.30)	0.63 (0.37-1.08)	1.58 (0.52-4.79)
Housewife	0.82 (0.61-1.10)	0.66 (0.42-1.03)	0.65 (0.44-0.96)*	1.05 (0.31-3.59)	1.96 (0.46-8.27)	0.71 (0.44-1.14)	1.36 (0.47-3.95)
Factory worker	1.18 (0.84-1.65)	0.79 (0.47-1.33)	0.63 (0.39-1.01)	1.87 (0.52-6.71)	4.77 (1.11-20.46)*	0.68 (0.38-1.24)	1.73 (0.54-5.57)
Company employee/self-employed	0.97 (0.73-1.30)	0.81 (0.52-1.26)	1.08 (0.75-1.57)	1.32 (0.39-4.49)	0.75 (0.17-3.27)	0.82 (0.52-1.29)	1.46 (0.50-4.23)
Other	1.18 (0.85-1.64)	0.70 (0.42-1.18)	0.92 (0.59-1.43)	0.87 (0.22-3.45)	0.90 (0.18-4.39)	1.27 (0.77-2.11)	2.16 (0.70-6.70)
Staff in administrative institutions	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Residential address							
Rural	0.88 (0.77-1.01)	1.08 (0.85-1.37)	0.62 (0.52-0.75)**	1.70 (0.98-2.94)	2.11 (1.33-3.35)**	0.71 (0.56-0.91)**	1.80 (1.07-3.04)*
Urban	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Family per capita annual income (yuan)							
< 10,000	1.01 (0.81-1.27)	0.90 (0.63-1.27)	0.97 (0.69-1.36)	0.80 (0.42-1.55)	1.52 (0.88-2.61)	0.73 (0.49-1.10)	1.04 (0.56-1.94)
10,000-14,999	0.89 (0.74-1.08)	0.67 (0.49-0.90)**	0.96 (0.73-1.28)	0.93 (0.54-1.58)	1.76 (1.09-2.85)*	0.57 (0.40-0.80)**	0.69 (0.40-1.21)
15,000-29,999	0.79 (0.67-0.94)**	0.70 (0.54-0.91)**	0.85 (0.66-1.08)	0.57 (0.34-0.94)*	1.60 (1.01-2.55)*	0.47 (0.35-0.63)**	0.76 (0.47-1.24)
30,000-49,999	0.80 (0.67-0.96)*	0.62 (0.47-0.83)**	0.92 (0.72-1.19)	0.78 (0.46-1.31)	1.12 (0.68-1.85)	0.65 (0.49-0.88)**	0.72 (0.43-1.21)
≥ 50,000	Reference	Reference	Reference	Reference	Reference	Reference	Reference

Note. [†] Physical and chemical risk factors on the questionnaire refer to the exposure to any risk factor related to physical and chemical risk factors. * Statistically significant (*P* < 0.05); ** Statistically significant (*P* < 0.01).

Table 2. Association between Demographic Characteristics and Exposure to Behavioral and Lifestyle Risk Factors

Demographic Characteristics	Behavioral/Lifestyle Risk Factors[†]	Cosmetic Use	Hair Dye or Perm	Pet Ownership	Pickled/Smoked Food Intake	Passive Smoking
Age (years)						
18-24	1.40 (1.08-1.81)*	1.73 (1.44-2.08)**	1.64 (1.37-1.97)**	0.91 (0.71-1.16)	1.04 (0.87-1.25)	1.11 (0.92-1.35)
25-29	1.38 (1.07-1.77)*	1.69 (1.41-2.03)**	1.48 (1.24-1.77)**	0.86 (0.68-1.10)	0.99 (0.83-1.18)	1.06 (0.88-1.29)
30-34	1.37 (1.04-1.82)*	1.39 (1.15-1.70)**	1.29 (1.06-1.56)*	0.90 (0.69-1.17)	0.96 (0.79-1.17)	1.07 (0.87-1.32)
35-47	Reference	Reference	Reference	Reference	Reference	Reference
Educational level						
Below primary/primary	1.03 (0.65-1.63)	0.57 (0.42-0.77)**	0.71 (0.53-0.96)*	1.10 (0.73-1.67)	1.02 (0.76-1.37)	1.18 (0.87-1.62)
Secondary	1.02 (0.83-1.25)	0.97 (0.86-1.10)	1.03 (0.91-1.17)	1.04 (0.87-1.24)	1.11 (0.98-1.25)	0.96 (0.84-1.10)
Tertiary/higher	Reference	Reference	Reference	Reference	Reference	Reference
Maternal occupation						
Farmer	1.46 (0.92-2.34)	1.17 (0.88-1.55)	1.09 (0.82-1.45)	0.94 (0.63-1.41)	0.84 (0.63-1.12)	0.99 (0.73-1.34)
Housewife	0.90 (0.58-1.39)	0.92 (0.70-1.20)	0.77 (0.59-0.99)*	0.88 (0.60-1.29)	0.77 (0.59-1.01)	1.09 (0.82-1.46)
Factory worker	1.27 (0.76-2.12)	1.24 (0.91-1.68)	1.30 (0.96-1.78)	0.97 (0.63-1.50)	0.86 (0.63-1.17)	0.93 (0.67-1.30)
Company employee/self-employed	1.19 (0.77-1.85)	1.41 (1.08-1.84)*	1.30 (0.99-1.69)	0.87 (0.59-1.28)	0.92 (0.70-1.19)	1.01 (0.76-1.34)
Other	1.20 (0.72-2.00)	1.04 (0.77-1.41)	1.11 (0.82-1.51)	1.08 (0.70-1.66)	0.77 (0.57-1.04)	1.41 (1.02-1.95)*
Staff in administrative institutions	Reference	Reference	Reference	Reference	Reference	Reference
Residential address						
Rural	0.85 (0.69-1.06)	0.69 (0.61-0.79)**	0.96 (0.84-1.09)	2.05 (1.65-2.54)**	1.07 (0.95-1.22)	1.46 (1.27-1.69)**
Urban	Reference	Reference	Reference	Reference	Reference	Reference
Family per capita annual income (yuan)						
< 10,000	0.54 (0.38-0.75)**	0.76 (0.62-0.94)*	0.86 (0.70-1.07)	0.85 (0.64-1.13)	0.72 (0.59-0.89)**	0.75 (0.60-0.94)*
10,000-14,999	0.64 (0.47-0.86)**	0.69 (0.58-0.82)**	0.65 (0.54-0.77)**	0.78 (0.62-0.99)*	0.80 (0.67-0.95)*	1.08 (0.90-1.30)
15,000-29,999	0.68 (0.52-0.90)**	0.73 (0.62-0.85)**	0.87 (0.74-1.02)	0.75 (0.60-0.92)**	0.83 (0.71-0.98)*	0.90 (0.76-1.06)
30,000-49,999	0.88 (0.65-1.18)	0.93 (0.79-1.10)	0.96 (0.81-1.13)	0.83 (0.66-1.03)	1.05 (0.89-1.23)	0.82 (0.69-0.97)*
≥ 50,000	Reference	Reference	Reference	Reference	Reference	Reference

Note. [†]Behavioral/lifestyle risk factors on the questionnaire refer to the exposure to any risk factor related to behavioral and lifestyle risk factors. *Statistically significant (*P* < 0.05); **Statistically significant (*P* < 0.01).

Table 3. Association between Demographic Characteristics and Exposure to Disease/Drug Risk Factors and Adverse Reproductive History

Demographic Characteristics	Disease/Drug Risk Factors[†]	Chronic Disease	Respiratory Infection	Adverse Reproductive History[‡]	Preterm Birth	Stillbirth	Abortion	Labor Induction
Age (years)								
18-24	1.31 (1.05-1.63)*	0.84 (0.59-1.21)	1.36 (1.06-1.75)*	0.25 (0.21-0.30)**	0.28 (0.11-0.73)**	0.29 (0.15-0.57)**	0.25 (0.21-0.31)**	0.33 (0.21-0.51)**
25-29	1.24 (0.99-1.54)	0.83 (0.58-1.18)	1.26 (0.98-1.62)	0.40 (0.34-0.48)**	0.46 (0.20-1.09)	0.54 (0.30-0.97)*	0.40 (0.34-0.48)**	0.59 (0.40-0.87)**
30-34	1.25 (0.99-1.58)	0.95 (0.65-1.40)	1.33 (1.01-1.73)*	0.65 (0.54-0.79)**	0.86 (0.35-2.09)	0.70 (0.37-1.33)	0.64 (0.52-0.77)**	1.02 (0.67-1.54)
35-47	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Educational level								
Below primary/primary	1.51 (1.08-2.10)*	1.32 (0.74-2.36)	1.29 (0.87-1.90)	1.73 (1.27-2.36)**	1.14 (0.12-10.88)	3.66 (1.05-12.83)*	1.52 (1.11-2.09)**	3.21 (1.46-7.08)**
Secondary	1.12 (0.97-1.30)	1.10 (0.83-1.46)	1.17 (0.99-1.38)	1.60 (1.39-1.83)**	2.38 (0.83-6.82)	2.94 (1.26-6.85)*	1.49 (1.30-1.71)**	2.78 (1.63-4.73)**
Tertiary/higher	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Maternal occupation								
Farmer	0.58 (0.43-0.79)**	1.27 (0.65-2.46)	0.50 (0.36-0.70)**	0.96 (0.70-1.30)	0.38 (0.07-2.13)	1.00 (0.21-4.83)	0.95 (0.70-1.31)	1.05 (0.43-2.53)
Housewife	0.54 (0.40-0.71)**	1.09 (0.58-2.07)	0.49 (0.36-0.67)**	0.92 (0.69-1.23)	0.42 (0.08-2.09)	0.83 (0.18-3.85)	0.97 (0.73-1.31)	0.55 (0.23-1.31)
Factory worker	0.73 (0.53-1.01)	0.86 (0.41-1.78)	0.75 (0.53-1.07)	0.97 (0.69-1.35)	0.11 (0.01-1.35)	1.17 (0.23-5.91)	1.02 (0.73-1.43)	0.59 (0.23-1.54)
Company Employee/self-employed	0.63 (0.47-0.83)**	1.04 (0.55-1.96)	0.56 (0.41-0.76)**	0.91 (0.68-1.21)	0.43 (0.09-2.21)	0.67 (0.14-3.17)	0.97 (0.72-1.30)	0.37 (0.15-0.90)*
Others	0.55 (0.39-0.77)**	1.01 (0.49-2.09)	0.50 (0.35-0.71)**	1.07 (0.77-1.49)	0.60 (0.09-3.97)	0.79 (0.14-4.36)	1.16 (0.83-1.62)	0.72 (0.27-1.90)
Staff in administrative institutions	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Residential address								
Rural	1.35 (1.16-1.58)**	1.50 (1.10-2.06)*	1.34 (1.12-1.59)**	1.08 (0.94-1.23)	1.27 (0.52-3.11)	2.00 (0.90-4.43)	1.05 (0.91-1.20)	1.36 (0.87-2.12)
Urban	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Family per capita annual income (yuan)								
<10,000	1.03 (0.82-1.29)	1.62 (1.04-2.51)*	0.82 (0.63-1.06)	1.05 (0.84-1.31)	4.40 (0.90-21.49)	0.85 (0.38-1.89)	0.98 (0.78-1.23)	1.17 (0.65-2.09)
10,000-14,999	0.73 (0.60-0.88)**	1.10 (0.73-1.64)	0.70 (0.56-0.87)**	0.93 (0.77-1.12)	2.19 (0.46-10.36)	0.48 (0.23-0.99)*	0.99 (0.82-1.20)	0.87 (0.52-1.46)
15,000-29,999	0.75 (0.63-0.90)**	1.11 (0.77-1.60)	0.73 (0.60-0.89)**	1.00 (0.85-1.18)	2.27 (0.52-9.90)	0.49 (0.26-0.94)*	1.02 (0.86-1.21)	1.01 (0.63-1.62)
30,000-49,999	0.86 (0.71-1.03)	1.28 (0.88-1.87)	0.86 (0.71-1.05)	1.05 (0.88-1.25)	2.95 (0.67-13.10)	0.87 (0.45-1.67)	1.07 (0.89-1.28)	1.24 (0.75-2.03)
≥50,000	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference

Note. [†] Disease and drug risk factors on the questionnaire refer to the exposure to any risk factor related to disease and drug risk factors. [‡] Adverse reproductive history on the questionnaire refers to the exposure to any risk factor related to previous adverse pregnancy. * Statistically significant ($P < 0.05$); ** Statistically significant ($P < 0.01$).

other hand, older pregnant women were more likely to have an adverse reproductive history. This is possibly due to the increased number of gravidity and parity times, decreased ovarian and uterine function, or increased probability of chromosomal abnormalities among older pregnant women[6].

Pregnant women with different educational levels suffered from exposure to different environmental risk factors. Feng's study[7] reported that a lower educational level was associated with occupational risk factors, such as exposure to pesticides and toxic chemicals, which was also supported by our study. A possible reason that may explain this finding is that pregnant women with low education may have limited awareness of self-protection, as a consequence of which they may not take adequate protective measures. We also observed that pregnant women with lower educational levels had an increased risk of adverse reproductive history. This may be due to reproductive health knowledge being less accessible to them, which may result in an increased number of adverse pregnancy outcomes[8]. This finding indicates that health education regarding personal protection and reproductive health is essential for pregnant women with low education.

It is important to notice that pregnant women working as staff in administrative institutions were more likely to be exposed to microwave ovens or induction cookers, while factory workers had higher exposure risk of fireworks production-related toxic substances; these findings indicate that pregnant women with different occupations have differential exposure to environmental risk factors according to their occupation, which required us to pay more attention to these differences. In addition, rural pregnant women had a higher risk of exposure to fireworks production-related toxic substances and environmental pollution. In contrast to our findings, a study[9] carried out in Texas reported that pregnant women living in urban environments were more likely to be exposed to hazardous waste sites and industrial facilities. Therefore, we should analyze different living environments to correctly identify the risk factors that pregnant women are more exposed to, and take targeted prevention and intervention measures. We also found that rural pregnant women had a relatively high exposure risk of passive smoking. A possible explanation for this finding could be that the smoking rate may be higher among Chinese rural residents than in residents in

urban areas[10], as tobacco control interventions and regulations have been widely implemented in public places of Chinese urban areas. Therefore, more strategies targeted at passive smoking among pregnant women in rural areas should be implemented.

This study has several limitations. First, exposure to environmental risk factors in this study was self-reported, thus, recall bias might be present. Second, quantitative data related to environmental risk factors exposure were not collected in this study. Third, the study was only conducted in the province of Hunan and, therefore, does not represent the total pregnant population in China.

Despite these limitations, this is a large population-based study carried out in China to explore the association between demographic characteristics and exposure to environmental risk factors. We found that the exposure rate to environmental risk factors was much higher than that of genetic risk factors; additionally, there were differences regarding exposure to environmental risk factors among pregnant women according to different demographic characteristics. These results can provide a scientific basis to identify at-risk populations who are more likely to be exposed to risk factors that might cause birth defects, which bear importance both in health education among pregnant women and primary prevention of birth defects.

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Supplementary Table S1. Data Collected from Participants

Category	Variables
Demographic characteristics	Maternal age, ethnicity, place of residence, educational level, occupation, and family per capita annual income.
Environmental risk factors	
Physical and chemical risk factors	X-rays contact, noise pollution, use of microwave oven or induction cooker, and exposure to toxic and hazardous substances, pesticides, fireworks production-related toxic substances, housing renovations, and environmental pollution.
Behavioral and lifestyle risk factors	Cosmetic use, hair dye or perm, pet ownership, intake of pickled or smoked food, alcohol use, active smoking, and passive smoking.
Disease and drug risk factors	History of chronic diseases, respiratory infections, and infectious diseases, and drug intake for the treatment of diseases, contraceptive drugs, and ovulation induction agents.
Adverse reproductive history	History of preterm birth, stillbirth, abortion, and labor induction.
Genetic risk factors	Maternal family history of birth defects and consanguineous marriage, paternal family history of birth defects and consanguineous marriage.

Supplementary Table S2. Demographic Characteristics of Pregnant Women (n = 10,163)

Demographic Characteristics	n	Percentage (%)
Age (years)		
18-24	3,404	33.5
25-29	4,551	44.8
30-34	1,631	16.0
35-47	577	5.7
Educational level		
Below primary/primary	220	2.2
Secondary	8,289	81.6
Tertiary/higher	1,654	16.3
Maternal occupation		
Farmer	1,380	13.6
Housewife	5,531	54.4
Factory worker	583	5.7
Company employee/self-employed	1,877	18.5
Other	501	4.9
Staff in administrative institutions	291	2.9
Residential address		
Rural	8,853	87.1
Urban	1,310	12.9
Family per capita annual income (yuan)		
< 10,000	714	7.0
10,000-14,999	1,756	17.3
15,000-29,999	4,593	45.2
30,000-49,999	2,267	22.3
≥ 50,000	833	8.2

Supplementary Table S3. Analysis of Exposure to Risk Factors among Pregnant Women (*n* = 10,163)

Risk Factors	Number of Exposed Women (*n* = 10,163)	Exposure Rate (%)	Order
Genetic risk factors	181	1.8	-
Environmental risk factors	9,558	94.0	-
Physical and chemical risk factors	2,619	25.8	3
Behavioral and lifestyle risk factors	9,018	88.7	1
Disease and drug risk factors	2,459	24.2	4
Previous history of adverse pregnancy outcomes	3,533	34.8	2
Numbers of exposure to risk factors			
0	599	5.9	-
1	1,325	13.0	-
2	1,992	19.6	-
3	2,333	23.0	-
4	1,765	17.4	-
≥ 5	2,149	21.1	-

Note. Pregnant women could have been exposed to more than one risk factor.

Supplementary Table S4. Exposure Rate Per Risk Factor and Their Ranking

Risk Factors	Number of Exposed Women (*n* = 10,163)	Exposure Rate (%)	Order
Physical and chemical risk factors			
X-rays contact	254	2.5	5
Noise pollution	768	7.6	2
Microwave oven or induction cooker use	**968**	**9.5**	**1**
Toxic and hazardous substances	222	2.2	6
Pesticides	58	0.6	8
Fireworks production-related toxic substances	545	5.4	3
Housing renovations	522	5.1	4
Environmental pollution	218	2.1	7
Behavioral and lifestyle risk factors			
Cosmetic use	5,296	52.1	3
Hair dye or perm	5,642	55.5	2
Pet raising	1,457	14.3	5
Pickled or smoked food intake	**5,682**	**55.9**	**1**
Alcohol use	162	1.6	6
Active smoking	56	0.6	7
Passive smoking	3,209	31.6	4
Disease and drug risk factors			
Chronic diseases	568	5.6	2
Respiratory infections	**1,783**	**17.5**	**1**
Infectious diseases	95	0.9	5
Drugs for disease treatment	172	1.7	3
Contraceptive drugs	148	1.5	4
Ovulation induction agents	80	0.8	6
Previous history of adverse pregnancy			
Preterm birth	61	0.6	4
Stillbirth	122	1.2	3
Abortion	**3,263**	**32.1**	**1**
Labor induction	317	3.1	2
Genetic risk factors			
Maternal family history of birth defects	74	0.7	1
Maternal family history of consanguineous marriage	49	0.5	3
Paternal family history of birth defects	50	0.5	2
Paternal family history of consanguineous marriage	39	0.4	4