

Risk factors for perinatal birth defects in Zhangye: a long-term hospital-based study

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Summary

Summary: To identify the factors contributing to birth defects using 18-year data for better intervention planning. **Materials and Methods:** A retrospective study was carried out using data collected from 169,155 perinatal infants at the city hospital of Zhangye from January 1996 to January 2012. **Results:** Among the infants, 289 had birth defects. Of them, 182 were detected before the birth with the incidence of 1.71‰ and detection rate of 62.98%; the perinatal mortality was 5.42%, while the mortality of defect infant was 175.42%. The most common defects were congenital heart disease, multiple finger (toe), cheiloschisis combined with palatogenesis, and ear abnormalities. Univalent conditional logistic regression analysis showed that there were eight statistically significant risk maternal factors contributing to the birth defects, including fever, viral infection, gestational diabetes mellitus, hypertension, other disease, antibiotics, other drugs, and pesticide exposure in early pregnancy. Multivariate logistic regression analysis showed that exposure to pesticides (OR = 14.43), viral infection (OR = 7.65), the use of other drugs (OR = 6.69), and antibiotics (OR = 6.55) were associated with the birth defects. **Conclusion:** It is clear that the birth defects can be reduced by taking precautionary measures before and during pregnancy, by prenatal diagnosis, and by proper treatment of the children with defects.

Key words: Birth defects; Prenatal screening; Prenatal diagnosis; Risk factor.

Introduction

Birth defects (BDs), also known as congenital anomalies, can cause fetal or infant death, loss of human life, childhood illness, and long-term disability. They bring tremendous mental stress and economic burden to the community and the family [1]. It is estimated that 6% of newborn have certain type of BDs [2]; among them, over 50% are likely due to genetic factors [3]. BD is reported to be associated with maternal medications and environmental exposures [4-7], pesticide exposure [8], viral infections [9], and maternal diseases [10, 11].

China is a country with a high incidence of BDs. BDs are related to many factors, including environmental factors whose impacts are less characterized, especially in the Loess Plateau, where the economic development is still low. Zhangye located in the Loess Plateau in Northwest China is one of the major cities in Gansu province. It is a city surrounded by large rural area and its population consists of 26 nationalities with over one million people. To objectively understand the status and dynamics of BDs and to identify factors associated with them, the authors retrospectively analyzed the perinatal infant data at the city hospital of Zhangye collected during 1996 to 2014. The results will help to develop strategies and measures to reduce BD.

Materials and Methods

Perinatal infants, including live, death, and stillbirth infants, were monitored for inpatients at 28 weeks of pregnancy between January 1996 and January 2014 at the People's Hospital of Zhangye, Gansu.

Infant information was collected according to the standards issued by the Chinese Birth Defects Monitoring Center. Infants with BD were recorded on Gansu Province BD report cards and Gansu Province BD registration forms. Quality control measures were taken to ensure data accuracy. Infants were subjected to a comprehensive examination and BDs were diagnosed accordance with the congenital malformation diagnosis standard issued by the National BD Monitoring Center. Information was collected using questionnaires. For the infant, the following information was collected: gender, date of birth, birth weight, gestational age, and parity. For the mother, name, age, nationality, family education, occupation, annual income per capita, residency, the number of pregnancy, health status, abnormal childbearing history, and the history of consanguineous marriage. For the materials that the mother contacted, 24 variables were recorded, including diseases, drugs used, alcohol, pesticides, other toxic chemicals, radiation, heated bed, sprouting potatoes, folic acid, calcium, iron, iodine, and vitamin supplements and inbreeding.

Data were entered using Epidate 3.02 and analyzed using statistical software SPSS 18 for single factor and multi factor conditional logistic regression. Statistical test was set at $\alpha = 0.05$.

Table 1. — *Birth defects, detection rates, and their proportion to overall birth defects.*

Rank	Birth defect	No. observed	Detected (%)	Proportion (%)
1	Congenital heart disease	35	1.21	12.11
2	Multi finger (toe)	26	0.90	9.00
3	Cheiloschisis combined with palatogenesis	23	0.80	7.96
4	Ear deformity	20	0.69	6.92
5	Anencephaly	17	0.59	5.88
6	Hydrocephalus	16	0.55	5.54
7	Spinal bifida	14	0.53	4.84
8	Visceral bareness	10	0.35	3.46
9	Rectal anal atresia or stenosis	8	0.28	2.77
10	Encephalocele	8	0.28	2.77
11	Esophageal atresia or stenosis	7	0.24	2.42
12	Limb shortening	7	0.24	2.42
13	Equinovarus	6	0.21	2.08
14	Everted gut	5	0.17	1.73
15	Cheiloschisis	4	0.14	1.38
16	Gastroschisis	4	0.14	1.38
17	Cleft palate	3	0.10	1.04
18	Neural tube defects	3	0.10	1.04
19	Hypospadias neural tube defects	2	0.07	0.69
20	Syndactyly and adactyly	2	0.07	0.69
21	Down's syndrome	2	0.07	0.69
22	Omphalocele	2	0.07	0.69
23	Others	65	2.25	22.49
	Total	289	17.09	

Results

A total of 169,155 infants were analyzed. Among them 289 had BD, including 187 (64.71%) males and 97 (33.56%) females. The remaining five (1.73%) were sexually undistinguishable. The overall BD rate was 1.71% and a detection rate of 62.98% was detected before birth. The male to female ratio was 2.05: 1. Two hundred and four cases (70.59%) were from rural areas and 85 cases (29.51%) from urban areas, and the ratio was 2.40: 1. The most common defects were congenital heart disease, multiple finger (toe), cheiloschisis combined with palatogenesis, and ear abnormalities (Table 1).

Univalent logistic regression showed that among the 24 variables, eight were statistically significantly associated with BDs. These risk factors included fever, viral infection, gestational diabetes mellitus, hypertension, other diseases, exposure to pesticides, administration of antibiotics, and other drugs in early pregnancy (Table 2).

To further analyze the contribution of each risk factor, the authors performed multivariate logistic regression analysis. The results showed that viral infection, other drugs, antibiotics, and pesticide exposure during early pregnancy were the major risk factors (Table 3).

Table 2. — *Univalent conditional logistic regression analysis of risk factors related to birth defects.*

Risk factor	β	SE	Wald	P	OR 95% CI
Fever ¹	2.71	1.03	6.87	0.01	14.99 1.98-31.56
Viral infection	2.130	0.61	12.31	0.01	8.420 0.56-27.69
Diabetes	2.14	1.04	4.33	0.03	8.89 1.14-71.04
Hypertension	2.18	1.05	4.34	0.04	9.00 1.14-71.04
Other diseases	2.08	1.06	3.84	0.05	8.00 1.01-63.96
Antibiotics	1.69	0.49	12.01	0.00	5.40 2.08-14.02
Other drugs	1.95	0.62	9.94	0.00	7.00 2.09-23.47
Pesticide exposure	2.18	1.05	4.34	0.04	9.00 1.14-71.04

¹ Conditions in the first three months of pregnancy.

Table 3. — *Multivariate logistic regression analysis of risk factors related to birth defects.*

Risk factor	β	SE	Wald	P	OR 95% CI
Pesticide exposure	2.67	1.22	4.79	0.03	14.43 1.32-57.63
Viral infection	2.04	0.82	6.19	0.01	7.65 1.31-40.10
Other drugs	1.90	0.81	5.59	0.02	6.69 1.38-32.31
Antibiotics	1.88	0.72	6.89	0.01	6.545 1.61-26.64

Discussion

Incidence of BD varies from time-to-time and from region-to-region. A better understanding of BD and its risk factors is vital to policy-makers and general public to develop and implement proper precaution, prevention, and treatment measures to minimize the negative impact. In this study, the authors analyzed hospital-based data collected over a 18-year period to draw an overall picture of BD in that region. Their analysis showed that exposure to pesticides, viral infection, and other drug and antibiotics use in early pregnancy are the main risk factors associated with BD in Zhangye area.

The authors also found that women exposed to pesticides are more likely to have infants with BD as compared with those who are not exposed [12]. It is possible that pesticides, such as lipid-soluble organochlorines, may accumulate in the fetus through the placenta. Therefore, it is highly recommended that pregnant women should take all possible measures to avoid coming into contact with pesticides.

Early studies showed that BDs are associated with viral infections, especially with rubella virus infection and cytomegalovirus, during the first three months of pregnancy [13]. The present study also indicated that the risk of BDs is higher in infected pregnant women than in uninfected women. In addition the authors found that other drugs (other than sulfa drugs, antibiotics, contraceptives, drugs, and sedatives) are associated with BD. These drugs are likely to penetrate through the placenta and reach the fetus, they might also affect the function of the placenta, maternal hormones or nutritional status to affect the development of fetus indirectly. Studies have shown that anti-cancer,

anti-seizure drugs, hormones, and other drugs are likely teratogenic [4] and total malformations and of the male genital organs are higher when the fetus is exposed to estrogen and progesterone *in utero* [14]. Therefore, it is highly recommended that no such drugs be taken during pregnancy.

Conclusion

The present analyses showed that a number of factors are associated with BDs, particularly exposure to pesticides, viral infections, and use of drugs and antibiotics. Proper intervention measures should be taken to reduce these factors that are likely helpful in reducing BDs and the burden on society and families.

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