

Preplanned Studies

Selected Structural Birth Defects — Shanxi Province, China, 2000–2019

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Summary

What is already known about this topic?

To reduce the high prevalence of neural tube defects (NTDs) in rural areas of the country, the Ministry of Health of China (currently known as the National Health Commission) initiated a nationwide folic acid supplementation program in 2009. The prevalence of NTDs have decreased from 118.9/10,000 births to 31.5/10,000 in northern China from 2000 to 2014.

What is added by this report?

Based on a population-based birth-defect surveillance system, the prevalence of selected structural birth defects in 5 counties in northern China decreased significantly from 182.8/10,000 births to 119.3/10,000 during the past two decades. Perinatal (28 gestational weeks or more) structural birth defects decreased from 83.9% of total birth defects in 2000 to 59.9% in 2019.

What are the implications for public health practice?

Improving the compliance of periconceptional folic acid supplementation, the fortification of staple foods with folic acid, and the health education surrounding early prenatal check-ups should be considered to further reduce the risk of birth defects in the population.

Birth defects, including congenital structural or functional abnormalities, remained a main cause of death among infants and represented a significant clinical and public health challenge (1). Periconceptional folic acid supplementation has been shown to effectively reduce the risk of pregnancies complicated with neural tube defects (NTDs) (2) and limb reduction (3). The prevalence of NTDs have decreased from 118.9/10,000 births to 31.5/10,000 in northern China from 2000 to 2014 and pre-perinatal (<28 gestational weeks) NTDs accounted for 60% of all NTDs (4). The trends of other birth defects among this population and the correlation with the folic-acid supplement program and population policy change had not been reported. This study aimed to examine

the trends of selected structural birth defects (Supplementary Table S1, available in <http://weekly.chinacdc.cn/>) in 5 counties in Shanxi Province during 2000–2019 based on a population-based birth-defect surveillance system. The results showed that the prevalence of selected structural birth defects in the study area decreased significantly from 182.8/10,000 to 119.3/10,000 during the past two decades.

Data from a population-based birth-defect surveillance system that covered 5 counties (Pingding, Xiyang, Taigu, Zezhou, and Shouyang) in Shanxi Province from 2000 to 2019 were analyzed in this study (Supplemental Figure S1, available in <http://weekly.chinacdc.cn/>). Details of the birth defects surveillance system were described in our previous publication (4). Briefly, the system was established in the early 2000s, and more than 20,000 births were covered each year. All pregnant women residing in the study area for more than 1 year were monitored. All livebirths or stillbirths of 28 or more complete gestational weeks and pregnancy terminations at any gestational age following the prenatal diagnosis of birth defects were included. The surveillance data covered more than 95% of live births and data quality was ensured. Information on the diagnostic criteria of birth defects (coded according to International Statistical Classification of Diseases and Related Health Problems, 10th revision), sex, gestational weeks, birth outcome and maternal residence was collected. The study protocol was reviewed and approved by the Institutional Review Board of Peking University.

The prevalence at birth of birth defects by year/period, by type, and by gestational week's group was compared using chi-squared tests. Perinatal prevalence (cases of 28 or more gestational weeks) and pre-perinatal prevalence (cases before 28 gestational weeks) were calculated, and 5 periods of time were demarcated according to population policy and public strategy. Two-tailed $p \leq 0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS package (version 18.0, SPSS Inc., Chicago, IL, USA).

From 2000 to 2019, a total of 293,573 births were covered and 4,748 infants with 5,845 cases of structural birth defects (an infant may have multiple birth defects) were recorded in the system.

Perinatal structural birth defects decreased from 83.9% of all birth defects in 2000 to 59.9% in 2019 (Figure 1A) (Pearson chi-squared tests: 62.958, $p < 0.05$) and the perinatal prevalence decreased dramatically from a peak of 139.6/10,000 births in 2003 to 74.7/10,000 in 2019 (Figure 1B).

Prevalence of nervous system defects was the highest and decreased from 169/10,000 births to 35/10,000 in the past two decades. Musculoskeletal system defects remained the second most common birth defect and fluctuated between 29/10,000 to 39/10,000. Cleft lip with or without cleft palate ranked third and decreased from 27/10,000 to 17/10,000 during 2000–2019 (Table 1, Figure 2A).

Among the selected birth defects, NTDs including anencephaly, spina bifida, and encephalocele and congenital hydrocephalus decreased significantly (Figure 2B). Anencephaly decreased from 62/10,000 live births in 2000–2003 to 9/10,000 in 2016–2019, and congenital hydrocephalus decreased from 29/10,000 to 8/10,000 during this period. The prevalence of spina bifida and encephalocele was estimated to decrease 75% during 2000–2019.

For congenital abnormalities of the nervous system, the prevalence decreased during 2000–2019, especially for perinatal prevalence, while the pre-perinatal prevalence increased from 73/10,000 births in 2000–2003 to 91/10,000 in 2004–2008, and then decreased to 75/10,000 in 2009–2011 to 30/10,000 in 2016–2019 (Figure 2C).

DISCUSSION

A population-based birth-defect surveillance system showed that the prevalence of selected structural birth defects in the 5 counties in Shanxi Province decreased significantly from 182.8/10,000 to 119.3/10,000 in the past two decades. After introduction of the massive folic acid supplementation program in 2009, both the perinatal and prenatal prevalences decreased significantly, especially for congenital abnormalities of the nervous system.

During the study period, premarital physical check-ups were changed from mandatory to voluntary in 2003, and a nationwide folic acid supplementation program was initiated in 2009. Corresponding with the reduction in the number of premarital check-ups,

the prevalence of birth defects before 28 weeks increased significantly in 2000–2003 compared to 2004–2008. After the change in policy, fewer women went to have a checkup and the opportunity for prophylaxis against birth defects was lost (5). Strengthening pre-pregnancy checkups and birth defect screening are important in preventing birth defects. To raise folic acid supplementation and to reduce the high prevalence of NTDs in rural areas of the country, the Ministry of Health of China (currently known as the National Health Commission) initiated a nationwide folic acid supplementation program in 2009 (6). The program provides folic acid supplements to all women who have a rural household registration (also known as hukou) and who plan to become pregnant. Our study showed that the prevalence of selected birth defects in 2009–2019 was significantly lower than that in 2000–2008, especially NTDs and cleft lip with/without cleft palate, which may be partly due to folic acid supplementation.

Our study found that the prevalence of defects of the nervous system in this area was still high as evidenced by the prevalence of 35/10,000 in 2019, which was significantly higher than national average level (7). Specifically, the prevalence of anencephaly in this study was found to be as high as 9/10,000 live births in 2016–2019 and 0.19/10,000 in Sichuan, China in 2010–2018. The prevalence of spina bifida was 15/10,000 in 2016 to 2019 in this study compared to 0.84/10,000 in Sichuan, China. The study conducted in Sichuan only captured perinatal pregnancies (more than 28 weeks), which may have contributed to lower prevalences as compared to this study (7). The folic acid supplementation rate increased significantly after 2009. However, most women began taking folic acid supplements after pregnancy, which was too late for the prevention of NTDs (6). Therefore, to improve the compliance of periconceptional folic acid supplementation, starting supplementation before the last menstrual period and supplementing for enough time are crucial for utilizing the maximum potential of the supplementation program. Fortifying staple foods with folic acid and improving health education on early prenatal check-up should be considered to further reduce birth defects risk in the population.

The current study did not find that the change in population policy had an effect on the epidemiology of birth defects. There were 3 major waves of adjustment on population policy during 2000 and 2019. Compared with the transition of “one child” to “two-child” policy from 2011 to 2013, the prevalence of

birth defects did not change significantly during the universal two-child policy started in 2016. So far, we did not observe the influence of population policy on

the risk of birth defects in the population. Studies revealed longer interpregnancy interval (IPI>60 months) increased the risk of having an infant with a

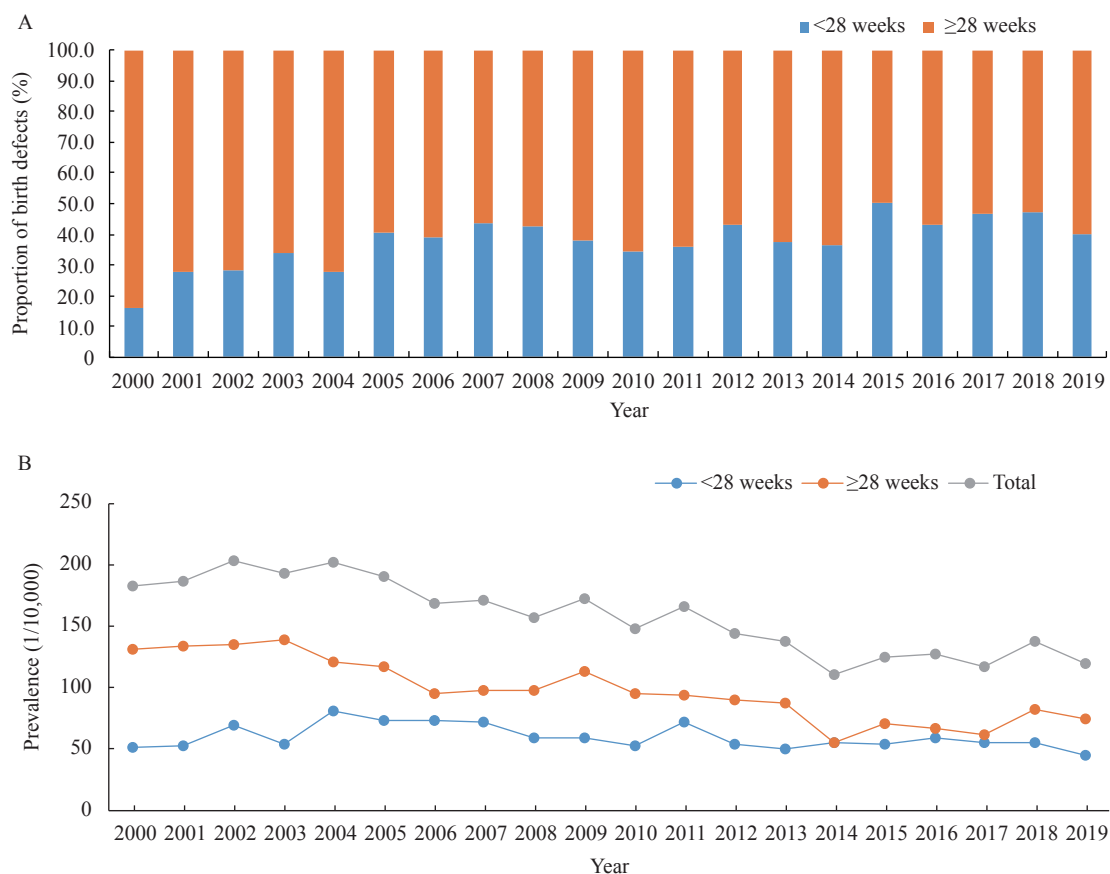


FIGURE 1. Selected structural birth defects by gestational weeks and year in 5 counties, Shanxi Province, China, 2000–2019. (A) Proportion of birth defects; (B) Prevalence of birth defects.

TABLE 1. Total number and prevalence (1/10,000) of birth defects by gestational weeks and system in 5 counties, Shanxi Province, China, 2000–2019.

ICD-10 code	Classification	Gestational weeks		
		<28 weeks	≥28 weeks	Total
1. Q00–Q07	The nervous system	1,987 (67.68)	1,206 (41.08)	3,193 (108.76)
2. Q10–Q18	Eye, ear, face and neck	1 (0.03)	139 (4.73)	140 (4.77)
3. Q20–Q28	The circulatory system	33 (1.12)	51 (1.74)	84 (2.86)
4. Q35–Q37	Cleft lip and cleft palate	81 (2.76)	614 (20.91)	695 (23.67)
5. Q38–Q45	The digestive system	4 (0.14)	119 (4.05)	123 (4.19)
6. Q50–Q56	Genital organs	0	79 (2.69)	79 (2.69)
7. Q60–Q64	The urinary system	3 (0.10)	7 (0.24)	10 (0.34)
8. Q65–Q79	The musculoskeletal system	122 (4.16)	816 (27.80)	938 (31.95)
9. Q80–Q89	Other congenital malformations	181 (6.17)	381 (12.98)	562 (19.14)
10. Q90–Q99	Chromosomal abnormalities	16 (0.55)	5 (0.17)	21 (0.72)
Total*		2,428 (82.71)	3,417 (116.39)	5,845 (199.10)

*The number of cases in this table was based on birth defect phenotypes, not the person. One person may have one more birth defects, so the total number of birth defects was greater than the cases.

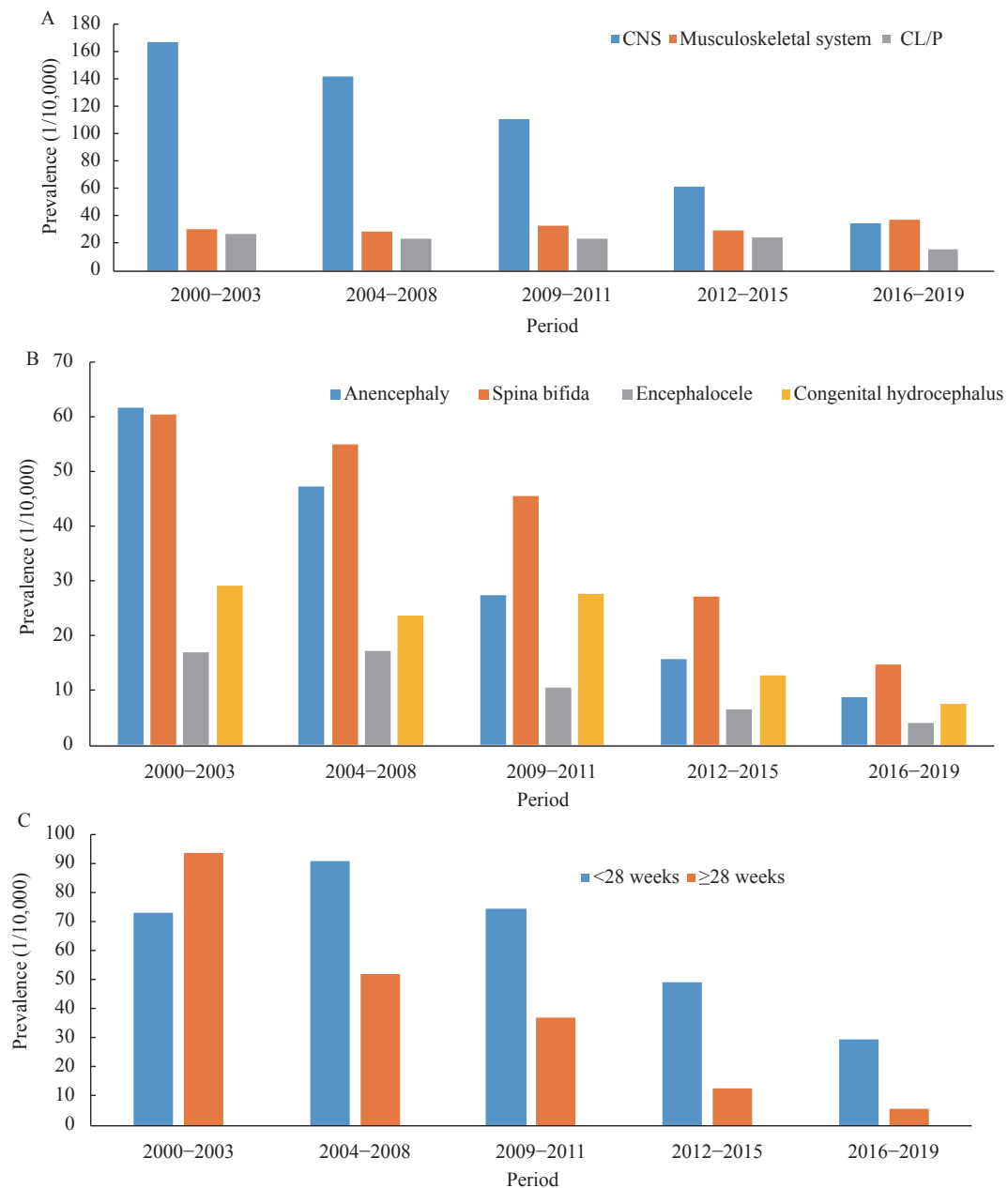


FIGURE 2. Prevalence of congenital abnormality by period in 5 counties, Shanxi Province, China, 2000–2019. (A) Pooled birth defects by system; (B) The nervous system defects by subtype; (C) The nervous system defects by gestational weeks. The 5 periods were divided according to population policy and public strategy, i.e., 2000–2003 (Period of mandatory pre-marital physical check-ups), 2004–2008 (Period of voluntary pre-marital physical check-ups and before folic acid supplementation), 2009–2011 (Period of after folic acid supplementation), 2012–2015 (Period of population policy transition) and 2016–2019 (Period of universal two-child policy). Abbreviations: CNS=central nervous system, CL/P=cleft lip and cleft palate.

birth defect (8). Advanced maternal age (AMA) increased the risk of aneuploidy, while AMA was associated with an overall decreased risk for major anomalies in the absence of aneuploidy (9). As more than 80% of subjects were from rural areas in the current study, age of childbearing was comparably young and the policy effect may not have been

significant. Following the enactment of the universal two-child policy, the proportion of women with AMA increased, and the risk of birth defects deserves more study in the future.

The rank of birth defects in this population was different from a study conducted in Sichuan, a southern province in China, that showed congenital

heart disease being the most prevalent birth defect (7). In our study, although the total prevalence of birth defects and the prevalence of several subtypes of birth defects decreased with time, congenital abnormalities of the nervous system, such as NTDs, was still the most prevalent birth defects, followed by defects of the musculoskeletal system, cleft lip and cleft palate, other system defects, and eye anomalies. The improvement of detection methods and changes in the diagnostic standard may have contributed to the increasing prevalence of congenital heart disease. The different patterns due to varying nutritional status, including but not limited to folate, among northern and southern China needs further study in the future.

This study was subject to some limitations. Due to the small selection area of a five mostly rural counties in Shanxi Province, the results were not generalizable to the province at large or to the country. The changes in policy may have affected different regions of the country differently and may have differing effects on urban populations.

Acknowledgements: We would like to express our appreciation to all the participants of the study. We express our profound gratitude to all hospital staff who collaborated with us from Pingding, Xiyang, Taigu, Zezhou and Shouyang counties. Specific thanks to Dr. Tao Xue who helped prepare the high-resolution imaging map of study areas.

doi: 10.46234/ccdcw2020.196

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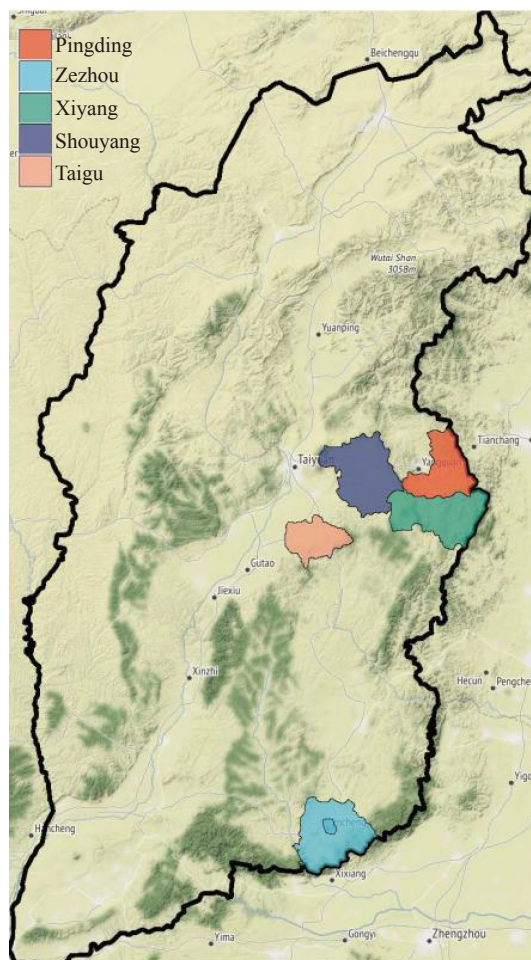
Submitted: August 05, 2020; Accepted: August 26, 2020

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SUPPLEMENTARY TABLE S1. Classification (ICD-10 code) of selected types of birth defects in the surveillance system.

ICD-10 code	Classification	Birth defects
1. Q00–Q07	The nervous system	01 Anencephaly
		02 Spina bifida
		03 Encephalocele
		04 Congenital hydrocephalus
2. Q10–Q18	Eye, ear, face and neck	08 Deformity of external ear
3. Q20–Q28	The circulatory system	23 Congenital heart disease
4. Q35–Q37	Cleft lip and cleft palate	05 Cleft palate
		06 Cleft lip
		07 Cleft lip with cleft palate
5. Q38–Q45	The digestive system	09 Esophageal atresia or stenosis
		10 Anorectal atresia or stenosis (without anus)
6. Q50–Q56	Genital organs	11 Hypospadias
7. Q60–Q64	The urinary system	12 hydronephrosis
8. Q65–Q79	The musculoskeletal system	13 Clubfoot left and right
		14 Multiple fingers (toes)
		15 Combined fingers (toes)
		16 Limb reduction [including missing fingers (toes) and split hands (feet)]
		17 Congenital diaphragmatic hernia
		18 Omphalocele
		19 Congenital dislocation of hip joint
9. Q80–Q89	Other congenital malformations	20 Gastroschisis
		21 Fetal conjoined twins
10. Q90–Q99	Chromosomal abnormalities	24 Others (state the name or detailed description of the disease)
		22 Down syndrome (trisomy 21)



SUPPLEMENTARY FIGURE S1. The 5 counties of a population-based birth defect surveillance system in Shanxi Province, China, 2000–2019.