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Neural tube defects in Beijing-Tianjin Area of China
Urban-rural distribution and some other epidemiological characteristics

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SUMMARY Records in the obstetric wards and nurseries of 18 hospitals were reviewed and studied epidemiologically, covering about 210 000 deliveries and 1000 cases of neural tube defects (NTD). All live and still births occurred in the period 1970—84. Following the NTD classification used by Koch (1984), our case series consisted of anencephalus 50·3%, spina bifida 44·2%, and NTD with other system defects 5·5%. Overall NTD prevalence rate at birth was 4 per thousand, obviously higher than those in most other countries. Marked urban-rural differences in NTD prevalence rate at birth were observed. The rate in rural areas after correction for selection bias was still as high as 7·25 per thousand. As compared with cities and suburbs, the relative risk of NTD born to mothers in rural regions was 2·4. The male-to-female ratios were much less than 1 for various kinds of NTD. Looking at the effect of maternal age and birth order simultaneously in 12 different settings, it can be seen that prevalence of NTD was moderately higher among second and third births to women aged $\leqslant 24$ and those $\geqslant 35$ years of age.

As the disease spectrum in many countries has been changing in recent decades, birth defects have become an increasingly important public health problem in many places. Today, scientific studies on and prevention of birth defects are imperative in China to facilitate implementation of the national family planning policy in order that babies born should be healthy and to strengthen the population's constitution. In 1981–2 obstetric colleagues in our First Teaching Hospital studying maternal child health care at a rural county in Beijing found an unexpectedly high prevalence rate of neural tube defects (NTD) at birth. We were thus prompted in 1983 to begin an epidemiological study on NTD in the Beijing-Tianjin Area. Epidemiological data concerning individual categories of birth defects, such as NTD, in this country have been very scarce. This paper describes the distribution of NTD by place and by person in the Beijing-Tianjin Area.

Material and methods

SOURCES OF DATA

These were log-books of obstetric departments and nurseries in hospitals of various levels (7 urban, 4 suburban, and 5 rural). Study subjects were all births, live and dead, normal and malformed, with gestational age over 28 weeks, and their mothers. Diagnosis of birth defects was usually made not later than seven days postpartum. Accumulated data were usually from 16 hospitals with more or less complete records (total births 208 801, NTD cases 925 within the period 1970—84). Some hospitals did not have records prior to 1979. Clinical data of an additional 75 perinatal NTD cases in two other hospitals in the same period were also used in analyses except in calculating the prevalence rates at birth, because exact numbers of corresponding total births in those two hospitals could not be obtained.

Four or sometimes three consecutive births in the same hospital of babies without defects immediately following the NTD baby on the same day were used as controls, yielding an average case/control ratio of 1:3.45.

CLASSIFICATION OF NTD

For the sake of comparing data from different places, we used the classification indicated by Koch *et al*[1] as follows: Anencephalus (AN) includes anencephalus alone, anencephalus with spina bifida, anencephalus with congenital hydrocephalus. Spina bifida (SB) includes spina bifida alone, spina bifida with congenital hydrocephalus, meningocele, meningomyelocele, encephalocele, myelocele, and

encephalocele with spina bifida. NTD with other system defects excludes NTD accompanied only by club foot. Simple hydrocephalus and spina bifida occulta were not considered as NTD.

METHODS OF ANALYSIS

Prevalence rate at birth is the most important index used consistently in this paper, and its denominator is the total number of births. General chi-square tests were often used. Joint effects of birth order and maternal age were analysed.

Because of the possibility of over-representation of rural NTD data, the rural NTD and all NTD rates were corrected for selection bias using previous experience in Shunyi County.[3]

Results

NTD CATEGORIES AND THEIR RELATIVE PROPORTIONS

Using the above classification, out of 1000 NTD cases, 503 were AN (50·3%), 442 SB (44·2%), and 55 NTD with other system defects (5·5%). AN-to-SB ratio is 1·14, quite close to 1·0, so it is similar to those in western countries but quite different from what Emanuel reported in Taiwan (SB/AN = 0·14, equivalent to AN/SB = 7).[2]

NTD PREVALENCE AT BIRTH IN BEIJING-TIANJIN AREA

From statistics of 208 801 total births (table 1), the overall NTD prevalence rate was as high as 4·4 per thousand, and that of the countryside was especially high at 9·91 per thousand. Since in rural regions of this area 35 to 50% of deliveries did not occur in the county hospitals from which our rural data came, rural NTD rates could have been biased to a certain extent by a tendency for women whose pregnancies are abnormal to be selected for hospital delivery. In the previous study in Shunyi County,[3] the prevalence of affected births among pregnancies in all women from the perinatal health care demonstration area was only 73·2% as high as among births in the county hospital. If this were true for all rural regions but for no others, the NTD rural rate would be 7·25 per thousand and the NTD overall rate 4·04 per thousand. These figures, though corrected, are still surprising (table 1). How wide an area this epidemic level of NTD covered is not clear, and is worthy of further investigation.

URBAN-RURAL DISTRIBUTION OF NTD

The overall NTD rate in the suburb was a little higher than that in the city region, but that of the countryside was remarkably higher than elsewhere, babies born to rural mothers having a relative risk of 2·4 compared to babies born in the city (7·25/2·98 = 2·4) if our estimate of the corrected rural rate is accurate. The corresponding rates in the city and suburb were only a matter of 30% different (3·98/2·98 = 1·30). Therefore it seems certain that there has been a real urban-rural difference of NTD rates in this area regardless of overall NTD or individual NTD categories viewed separately (table 1).

PREVALENCE RATES BETWEEN BEIJING AND TIANJIN

These rates were compared (urban and rural separately), and data from comparable hospitals showed that, as expected, there were no substantial or statistically significant differences in either overall birth defects prevalence or NTD prevalence rates between Beijing and Tianjin.

Table 1 *Neural tube defects prevalence rates at birth per thousand, Beijing-Tianjin Area, urban-rural comparison*

	Number of hospitals	*Total births*	*Prevalence rate at birth per thousand*			
			NTD total	*AN*	*SB*	*Other NTD*
City	7	90 472	2.98 (270)	1.36 (123)	1.38 (125)	0.24 (22)
Suburb	4	87 350	3.98 (348)	1.81 (158)	1.97 (172)	0.21 (18)
Rural	5	30 979	9.91 (307)	5.81 (180)	3.68 (114)	0.42 (13)
Total	16	208 801	4.4 (925)	2.21 (461)	1.97 (411)	0.25 (53)
χ^2test	–	–	p<0.001	p<0.001	p<0.001	

*Figures in parentheses are numbers of cases

MALE-TO-FEMALE RATIO OF NTD CASES

Statistics from 795 cases of NTD showed that in this area the sex ratio for overall NTD cases, for anencephalus, for spina bifida, and for complicated NTD were 0·497, 0·358, 0·648, and 0·792 respectively. In all cases females predominated, similar to western data.

EFFECT OF BIRTH ORDER AND MATERNAL AGE

There were 993 cases of NTD and 3429 controls whose birth order and maternal age were recorded. Their distribution in terms of these variables is shown in table 2. The odds ratios in the table were calculated relative to all births of known mothers' age and birth order. The p values (of χ^2) indicate the probability of encountering by chance such odds ratios in respective cells.

Within each birth order group (especially second and later births) the trend of risk with maternal age group was U-shaped. Within each maternal age group (especially the youngest and the oldest) second births were at higher risk than first births, but the trend between second and later births was variable.

Discussion

Statistics from 208 801 total births in the hospitals of the Beijing-Tianjin area revealed a remarkably high NTD prevalence rate of 4·04 per thousand at birth, and a rate of 7·25 per thousand in rural hospitals. These rates are really high, because in the last one or two decades, the NTD prevalence rates at birth in many countries have been declining, for example to as low as 0·6 per thousand.[2 4]

According to published material and presented data in China, NTD prevalence at birth in Guanzhow, Wuhan, Jiangxi, Shanghai, Anhui, and other places in the south of China varied from 0·6 to 2·4 per thousand. For instance, Liu reported NTD prevalence at birth in Shanghai to be 0·63 per thousand based on 44 710 live births of 10 consecutive years.[5] Data from the north of China (Shandong, Shanxi, Hopei, Beijing, and Henan) and north-east of China (Harbin, etc) all revealed NTD prevalence rates of 5·9 to 13 per thousand, higher than our 4·04 per thousand. For example, Shanxi reported a rate of 7 per thousand, based on 48 831 births.[6] One can then infer that NTD may be more prevalent in the northern than in the southern parts of China. However, more studies are needed to clarify this point.

Our data show that in the Beijing-Tianjin Area, whose inhabitants are almost exclusively Hans, NTD occurred more frequently in rural areas than in the city and suburbs. It is obvious that this urban-rural distribution cannot be accounted for by genetic or ethnic factors. Urban-rural distribution of NTD is a topic that has not generally been well studied. It has been reported that in England and Wales, Northern Ireland, the USA, and Quebec, NTD was more prevalent in cities than in the countryside.[2] Imaizumi,[8] in his study of NTD, found no urban-rural difference in NTD mortality in Japan. This discrepancy is not unexpected, because a different culture and a different life style and socioeconomic status exist in different

Table 2 *Joint effects of birth order and maternal age on occurrence of NTD (18 hospitals)*

Maternal age (years)		*Birth order*		
		1	2	3+
17–24	Cases	130	47	21
	Controls	404	70	50
	Odds ratios*	1.11	*2.32*	1.45
	p	>0.25	<0.001	>0.10
25–29	Cases	443	50	15
	Controls	1730	150	95
	Odds ratios*	0.88	1.15	*0.55*
	p	0.05<p<0.10	>0.30	<0.05
30–34	Cases	59	57	22
	Controls	257	183	62
	Odds ratios*	0.79	1.08	1.23
	p	>0.10	>0.50	>0.30
35+	Cases	66	46	37
	Controls	246	116	66
	Odds ratios*	0.93	1.37	*1.94*
	p	>0.50	0.05<p<0.01	<0.01

*Relative to all births of known maternal age and birth order (993 cases, 3429 controls)

nations. It seems that the urban-rural differences in NTD prevalence did not result from natural geographic variations but rather from different cultural and social aspects of city and rural settings. British and other European studies showed that NTD occurred more frequently in social classes 4 and 5 than in classes 1 and 2.[2 7] There are also some reports which suggest an association between NTD and poor diet of expectant mothers.[2 7] Whether the preponderance of NTD in rural regions of the Beijing-Tianjin Area reflects a lower socioeconomic and nutritional status needs further investigation.

Although the birth prevalence of NTD in this area is quite high, the current findings do not show a higher risk of NTD in first births, which is characteristic of other high-prevalence countries, such as England, Scotland, and Hungary. Our data with respect to the effect of birth order and maternal age are similar to the pattern in low-prevalence countries such as Israel and Finland.[2 7] The reason for this is not known at present.

Data presented in this paper are considered to be of high validity, because (1) NTDs are easily diagnosed, (2) data are from the medical records of a number of hospitals of various levels over a considerable period of time, and (3) a large sample has been taken. However, only three hospitals in Tianjin were involved in this study, so the representativeness for Tianjin is not satisfactory.

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