

Epidemiology of neural tube defects in northern Iran, 1998–2003

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وبائيات عيوب الأنبوب العصبي في شمال إيران، 1998–2003
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الخلاصة: تم في إطار هذا البحث تقدير معدلات عيوب الأنبوب العصبي في مستشفى للإحالة في مدينة غورغان، بشمال جمهورية إيران الإسلامية، وعلاقة هذه العيوب بالجنس، والأصل الإثني للأم، وعمر الأم، والفصل. ولوحظت 109 حالات من بين 37 951 ولادة في الفترة 1998–2003، أي بمعدل انتشار 28.7 حالة لكل 10 000 ولادة (24.8 حالة لكل 10 000 من الذكور، و32.8 حالة لكل 10 000 من الإناث). وبلغ هذا المعدل 40.5 لكل 10 000 من المنتمين للعرق التركماني، 25.2 بين المنتمين للعرق الفارسي، و30.8 بين المنتمين للعرق السستاني. وكان معدل حدوث السنسنة المشقوقة 16.3، وانعدام الدماغ 11.3 لكل 10 000 شخص. وكان معدل المصابين من حديثي الولادة أعلى ما يكون في حالة زيادة عمر الأم على 35 عاماً (50.7 لكل 10 000). وكانت ذروة الانتشار في شهر كانون الأول/ديسمبر.

ABSTRACT We determined the rates of neural tube defects at a referral hospital in Gorgan, north Islamic Republic of Iran, and the relations of these abnormalities to sex, maternal ethnicity, maternal age and season. During 1998–2003, there were 109 cases among 37 951 births, a prevalence of 28.7 per 10 000 (24.8 and 32.8 per 10 000 among males and females respectively). The rates in Turkmen, native Fars and Sistani ethnic groups were 40.5, 25.2 and 30.8 per 10 000 respectively. The rates of spina bifida and anencephaly were 16.3 and 11.3 per 10 000 respectively. The rate of affected newborns was highest in mothers aged over 35 years (50.7 per 10 000). The peak prevalence was in December.

Épidémiologie des malformations du tube neural dans la région Nord de l'Iran, 1998-2003

RÉSUMÉ Nous avons déterminé le taux de malformations du tube neural dans un hôpital de recours de Gorgan, ville située au nord de la République islamique d'Iran, et caractérisé la relation entre ces malformations et des paramètres tels que le sexe de l'enfant, l'origine ethnique de la mère, l'âge maternel et la saison. Au cours de la période 1998-2003, sur les 37 951 naissances enregistrées, il a été recensé 109 cas de malformations du tube neural, soit une prévalence de 28,7 pour 10 000 naissances (à savoir respectivement 24,8 et 32,8 cas pour 10 000 naissances de sexe masculin et féminin). Dans les trois groupes ethniques Turkmène, Farsi et Sistani, ces taux étaient respectivement de 40,5, 25,2 et 30,8 pour 10 000 naissances. Le spina bifida et l'anencéphalie représentaient respectivement 16,3 et 11,3 cas pour 10 000 naissances. La fréquence des malformations du tube neural s'est avérée plus importante chez les nouveau-nés de mères âgées de plus de 35 ans (50,7/10 000 naissances). La prévalence maximale a été observée en décembre.

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Introduction

Neural tube defects (NTD) result in congenital malformations of the nervous system, the most common of which are anencephaly, spina bifida and encephalocele. They are the result of multifactorial disturbances in embryonic neurulation [1]. Numerous risk factors have been identified for NTD. Exposure to methotrexate, valproic acid or aminopterin, maternal diabetes, hyperthermia, low socioeconomic status, and lack of folate have been shown to increase the risk of NTD. Also, genetic factors are believed to be important [2–5].

The prevalence of NTD at birth varies considerably by country, geographic zone, and ethnic and racial group; it ranges from as high as 1 case in 100 births in some regions of China to about 1 case in 2000 or less in some Scandinavian countries. In many countries the prevalence is approximately 1 in 1000 births [5–8].

Previous studies on NTD have been carried out in some parts of the Islamic Republic of Iran. In a study on 13 037 births in the capital, Tehran (1969–78), 17.6/10 000 newborns had NTD [9]. In another study of 8585 deliveries in Hamadan (1991–97) (a north-west province), the prevalence of NTD was 50.1/10 000 [10] and in Canadajh–Kordestan (another north-west province), out of 14 915 births, 55.0/10 000 newborns had NTD [11].

NTD may lead to spontaneous abortion, stillbirth, death in early infancy or a lifetime of disability. In view of the significant health costs of NTD it important to have baseline data of the prevalence of NTD in every region. This study was done in a referral hospital in the north of the Islamic Republic of Iran during 6 years (1998–2003) to determine the prevalence of different types of NTD and the relations of these abnormalities to factors including

sex, maternal ethnicity, maternal age and season.

Methods

This descriptive cross-sectional study was carried out in Dezyani teaching hospital in Gorgan, the capital city of Golestan province, north Islamic Republic of Iran. The hospital serves as a referral centre for obstetric and gynaecologic problems and a prenatal intensive care unit for all other hospitals and clinics in the south-east of the Caspian Sea border (Golestan province). The region has a population of about 1.5 million and covers an area of about 20 460 km². Dezyani hospital is one of 17 hospitals and there are more than 500 primary health centres in the region. As a result, patients in this catchment area requiring transfer for the purpose of specialized investigations and treatment (obstetrics and gynaecology) must be referred to Dezyani hospital.

All live and stillbirth newborns delivered in the hospital from January 1998 through December 2003 from mothers residing in Gorgan province were screened for congenital malformations. NTD were defined according to the *International classification of diseases*, version 10. Stillbirths referred to all fetal deaths after 24 weeks or longer gestation. It was not possible in this study to record data about abortions. All NTD rates were calculated per 10 000 births.

Demographic characteristics and general information of all of the neonates and their parents—sex, date of birth, kind of NTD, mother's age and ethnicity—were recorded in the medical chart. Other variables such as consanguineous marriage and residence of parents were recorded only for neonates with NTD. Three ethnic groups (native Fars, Turkmen and Sistani) were defined. The native Fars groups are

the predominant inhabitants of the region. The Turkmen migrated from other parts of central Asia around 250 years ago and have a rate of interracial marriage of nearly 100%. The Sistani are immigrants from the Iran–Pakistan–Afghanistan border from half a century ago.

All data were analysed with *SPSS* software and were evaluated and compared with the chi-squared test. A *P*-value of 0.05 or less was considered statistically significant.

Results

Between 1998 and 2003 there were 37 951 births in Dezyani teaching hospital, Gorgan, with 109 newborns and stillbirths recorded with NTD. The prevalence at birth of NTD during the 6-year period was therefore 28.7 per 10 000 births. There were 48 males and 61 females; the rate of NTD was 24.8/10 000 and 32.8/10 000 in males and

females respectively (no significant difference) (Table 1).

Out of the 109 NTD cases, 62 had spina bifida, 43 were anencephalic and 4 had encephalocele. The corresponding prevalence for spina bifida was 16.3/10 000 births (13.9 and 18.8/10 000 for males and females respectively), for anencephaly 11.3/10 000 (9.3 and 13.5/10 000 for males and females) and for encephalocele 1.1/10 000 (1.5 and 0.5/10 000 for males and females).

Table 1 shows the rate of NTD by mother's age; the highest rate of NTD was 50.7/10 000 in newborns with mothers aged ≥ 35 years.

The NTD rates were 40.5/10 000, 25.2/10 000 and 30.8/10 000 for mothers of Turkmen, native Fars and Sistani ethnic groups respectively (no significant difference). This study shows 36 (33.0%) of the parents with affected newborns had consanguineous marriages. Also 63% of the parents resided in rural areas and 37% in urban areas.

Table 1 Prevalence of neural tube defects (per 10 000 births) by sex, mother's age and ethnic group, 1998–2003

Variable	Total no. of births	Type of defect						Total No. /10 000	χ^2	<i>P</i> -value	
		Spina bifida		Anencephaly		Encephalocele					
		No.	/10 000	No.	/10 000	No.	/10 000	No.	/10 000		
<i>Sex</i>											
Male	19 370	27	13.9	18	9.3	3	1.5	48	24.8	2.13	0.14
Female	18 581	35	18.8	25	13.5	1	0.5	61	32.8		
<i>Mother's age (years)</i>											
15–19	5 161	4	7.8	6	11.6	2	3.9	12	23.3	3.86	0.15
20–34	30 817	52	16.9	33	10.7	2	0.6	87	28.2		
≥ 35	1 973	6	30.4	4	20.3	–	–	10	50.7		
<i>Mother's ethnic group</i>											
Native Fars	25 439	36	–	25	–	3	–	64	25.2	3.96	0.14
Turkmen	5 686	12	–	11	–	–	–	23	40.5		
Sistani	6 826	13	–	7	–	1	–	21	30.8		
<i>Total</i>	37 951	62 ^a	16.3	43	11.3	4	1.1	109	28.7		

^aThe ethnicity of one newborn was not recorded.

Figure 1 shows the rate of NTD each year. The highest rate was in the year 2000 (36.0/10 000). Seasonal variations during the 6-year period were observed. The rate of NTD in October to March (33.0/10 000 births) was higher than July to June (24.0/10 000 births) ($\chi^2 = 2.42$, $df = 1$, $P > 0.05$). The peak prevalence occurred in December.

Discussion

Our study showed a rate of NTD in this referral hospital in the Islamic Republic of Iran of 28.7/10 000 births. In this research we could not study abortions and therefore our results may be underestimated. Our rate is higher than studies in other countries such as Canada where it was 1.41/1000 [8], in South Africa 1.74/1000 [12], in Germany 15.0/10 000 [13], in the north of England 17.9/10 000 [14], in the north of France 10.9/10 000 [15] and in the United States of America (USA) 9.3 to 14.6/10 000 [5]. The rate is lower than that of China which was

6.0/1000 [16], in Turkey 30.1/10 000 [3] and in north-west of the Islamic Republic of Iran (Hamadan) 50.1/10 000 [10]. These variations in different studies could be explained by the influence of racial, ethnic and social factors in various parts of the world, which are commonly explained as genetic disorders. Geographical, nutritional and socioeconomic and biological factors could also be involved. Other reasons for these variations in birth defect prevalence are the type of sample (referral hospitals would be expected to have higher rates) and method of diagnosis).

The rates of NTD in different ethnic groups showed that the Turkmen had the highest rate at 40.5/10 000 but among native Fars it was 25.2/10 000 and among Sistani it was 31.0/10 000. Studies by other researchers also show different NTD rates among different races [5,17,18], suggesting that race and ethnicity may be a factor in the rate of NTD [19].

Spina bifida was the most common NTD in our study, which agrees with

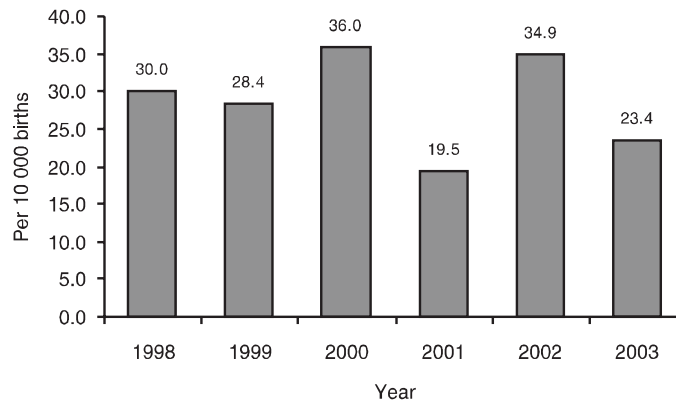


Figure 1 Annual rates of neural tube defects (/10 000 births)

other studies [20,21], followed by anencephaly and encephalocele. The rate of cystic spina bifida in our study population was 16.3/10 000, which is higher than 6.2/10 000 in France [22], 7.1/10 000 in Texas [5] and 1.09/10 000 in Saudi Arabia [23]. It should also be mentioned that our rate is higher than another study in Tehran (central Islamic Republic of Iran) with 3.8/10 000 [9] and in Hamadan (north-west province) with 6.98/10 000 [10]. The rate of anencephaly in our study was 11.3/10 000, which is higher than the other studies such as 6.0/10 000 in South America [24], 6.4/10 000 in Texas [5] and 8.0/10 000 in Tehran [9]. But the rate in our study was lower than in Hamedan with 15.6/10 000, China with 87.0/10 000 and Turkey with 16.4/10 000 [10]. The rate of encephalocele (1.1/10 000) was similar to a study in the USA (1.03/10 000) [5].

Regarding sex differences, our results indicate that the rate of NTD was higher in females than males (male to female ratio = 0.76), as reported by other researchers [5,25,26]. The male to female ratio was 0.69 for anencephaly and 0.74 for spina bifida, which is also comparable to other studies [5,9,17,22–24]. For example, in the USA the ratio for all NTD was 0.62, for anencephaly 0.54 and for spina bifida 0.68 [5].

Our research showed that the highest rate of affected newborns was in mothers aged ≥ 35 years (50.7/10 000), with 23.3/10 000 in mothers aged 15–19 years and 28.2/10 000 aged 20–34 years. Our observation of a linear relation between the rate of NTD and increasing maternal age is different from other studies which show a higher risk among younger mothers [27] or, more commonly, a U-shaped curve with higher rates in mothers aged under 19/20 years and over 35 years [5,12,22,28]. Thus age is a complex risk factor in NTD and this issue needs more investigation.

In this study a seasonal variation was observed and the rate of NTD was higher in the October to March period with a peak in December. In a study in Ireland [27] the rate was higher in January–June (28.0/10 000) compared with July–December (23.2/10 000). Also in Ireland the peak was in April [27].

Some research has shown that the rate of consanguineous marriage is high in NTD births [21,23]. In our study 33% of parents with affected newborns had consanguineous marriage, although this rate is lower than in Saudi Arabia (89% of the spina bifida parents) [23] and higher than in South Africa [12]. Another study in the north-west of the Islamic Republic of Iran indicated that the rate of consanguinity among parents with healthy infants was 23% [29]. The possibility that consanguinity could be a risk factor for NTD in a population requires further research.

In this study 63% and 37% of parents with affected newborns lived in rural and urban areas respectively. A greater prevalence of NTDs at birth has been shown for rural areas compared with urban areas [30,31]. A report from China (1988–1991) indicated the prevalence of NTD in rural areas (44.3/10 000) was 3 times higher than urban areas (14.4/10 000) [32]. It may be due to factors such as high population growth rates and socioeconomic factors.

According to our findings ethnicity and interfamilial marriage may play a role in the NTD rate in this region of the Islamic Republic of Iran, although there could also be effects of environmental factors such as exposure to toxic agricultural substances and nutritional factors such as folate deficiency. So further investigations are needed, and we recommend that a central registry be set up to record NTD occurring in the south-east Caspian Sea region of the country.

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