

# Epidemiologic aspects of neural tube defects in South East Iran

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## ABSTRACT

**Objectives:** To investigate the rate of neural tube defects (NTDs) and their relation to gender, maternal age, consanguineous marriage, season, and drug consumption in Birjand, Iran.

**Methods:** This research was carried out on 16,785 live or stillborn newborns in Birjand, Iran from April 1997 to December 2001.

**Results:** The rate of NTDs was 2.97 per 1000. This rate was 1.97 per 1000 in males, and 3.55 per 1000 in females. The rate of anencephaly was 1.37 per 1000, and spina

bifida was 0.88 per 1000. We found that 32% of mothers with affected newborns had taken drugs during the first trimester of pregnancy, 90% of mothers did not consume folate before and during the first trimester, and 54% of parents had consanguineous marriage.

**Conclusion:** We concluded that folate deficiency, usage of drugs during pregnancy, and consanguineous marriage may play a role of predisposition to NTD.

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Neural tube defects (NTDs) result in congenital malformations of the nervous system and may lead to spontaneous abortion, stillbirth, or death in early infancy, or a lifetime of disability.<sup>1</sup> Neural tube defects, the most common of which are anencephaly, spina bifida, and encephalocele, result from multifactorial disturbances in embryonic neurulation.<sup>2</sup> Numerous risk factors have been identified for NTDs. Exposure to methotrexate, valproic acid, aminopterin, maternal diabetes, hyperthermia, low socioeconomic status, and lack of folate have been shown to increase the risk of NTDs.<sup>1,3-11</sup> Also, genetic risk factors are believed to be important.<sup>12</sup> The prevalence of NTD at birth varies considerably by country, geographic zones, ethnic and racial groups, and ranges from as high as 1 case in 100 births in some regions of China, to approximately 1 case in 5000 or less in some Scandinavian countries. In many countries, the

prevalence is approximately 1 in 1000 births.<sup>10</sup> We carried out this study in Birjand, in the south-east of the Khorasan province, Iran (Afghanistan border), to ascertain a relationship between the NTDs and the following factors; sex, maternal age, consanguineous marriage, season, drugs consumption, history of disease, and also to investigate the rate of NTDs.

**Methods.** This descriptive and cross-sectional study was carried out on 16,785 live or stillborn newborns from April 1997 to December 2001 in 2 hospitals (Imam Reza and Mehr) in Birjand, South East Iran. Cases were defined as women residing in Birjand who delivered live or stillborn newborns with neural tube defects (ICD-9). Demographic characteristics of the neonates and their parents such as sex, date of birth, type of NTD, mother's age, consanguineous marriage, drug consumption, mother's diseases, and history of

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**Table 1** - The rate of type of NTDs per 1000 birth.

NTDs	No.	(%)	Rate per 1000
Anencephaly	23	(46)	1.37
Spina bifida	8	(16)	0.47
Spina bifida & hydrocephalus	7	(14)	0.41
NTD & other anomalies	6	(12)	0.36
Encephalocele	3	(6)	0.18
Iniencephaly	3	(6)	0.18
<b>Total</b>	<b>50</b>	<b>(100)</b>	<b>2.97</b>
NTDs - Neural tube defects			

malformed newborn, were recorded in the medical chart. All NTDs rates were calculated per 1000 births. The data were analyzed by SPSS, Version 10. Chi-square, fisher exact and student's t-test was applied whenever necessary. The *p*-value of  $\alpha=0.05$  or less was considered statistically significant.

**Results.** During 1997-2001, there were 16,785 births in 2 hospitals. Among this sample population, there were 8609 males, 8154 females and 22 ambiguous genitalia. During the period under consideration, we found 50 live and stillborn newborns with NTDs.

These were made up of 29 females, 17 males and 4 newborns with ambiguous genitalia. The rate of NTDs was 2.97 per 1000 births. The rate of NTDs was 1.97 per 100 for males and 3.55 per 1000 for females. The female/male ratio of NTDs was 1.71. This difference was not statistically significant. The distribution of type of NTDs is depicted in **Table 1**. In this study, the rate of anencephaly in the total population was 1.37, and spina bifida was 0.88 per 1000. The mean age of mothers was  $28\pm6$  and of fathers was  $32\pm9$  years. Twenty-seven (54%) of the 50 offspring were derived from consanguineous marriage and the parents were not related in the other 46% (**Table 2**). Thirty-two percent of the newborns with NTDs were born in winter. In spring, 26% were born, 14% in summer, and 28% of affected newborns were born autumn. In this study, 32% of mothers with malformed newborns had taken drugs during the first trimester of pregnancy, and 46% of them had disease during pregnancy (**Table 2**). In addition, 90% of mothers' with NTD newborns did not consume folate before and during the first trimester of pregnancy.

**Discussion.** Our results indicate that the rate of NTDs was 2.97 per 1000, which is higher than other studies from Canada at 1.41/10000,<sup>13</sup> South

**Table 2** - Distribution of consanguineous marriage, type of delivery, disease and drug consumption in mothers with affected newborn according to type of NTDs.

NTDS Risk factors	Anencephaly N=23	Spina bifida N=8	Encephalocele N=3	Iniencephaly N=3	Spina bifida & Hydrocephalus N=7	NTD & other anomalies N=6	Total N=50
	No. (%)						
<b>Consanguineous marriage</b>							
No	11 (47.8)	4 (17.4)	2 (8.7)	2 (8.7)	2 (8.7)	2 (8.7)	<b>23</b>
Yes - type 3,4	8 (40)	4 (20)	1 (5)	1 (5)	4 (20)	2 (10)	<b>20</b>
- type 5,6	4 (57.1)	0 (0)	0 (0)	0 (0)	1 (14.3)	2 (28.6)	<b>7</b>
<b>Type of delivery</b>							
Vaginal	19 (59.4)	4 (12.5)	2 (6.3)	0 (0)	2 (6.3)	5 (15.6)	<b>32</b>
Cesarean section	4 (22.2)	4 (22.2)	1 (5.6)	3 (16.7)	5 (27.8)	1 (5.6)	<b>18</b>
<b>Disease during pregnancy</b>							
No	15 (55.6)	4 (14.8)	1 (3.7)	1 (3.7)	3 (11.1)	3 (11.1)	<b>27</b>
Yes - FUO	1 (14.3)	2 (28.6)	1 (14.3)	0 (0)	2 (28.6)	1 (14.3)	<b>7</b>
- diabetes mellitus	0 (0)	1 (33.3)	0 (0)	0 (0)	1 (33.3)	1 (33.3)	<b>3</b>
- other	7 (53.8)	1 (7.7)	1 (7.7)	2 (15.4)	1 (7.7)	1 (7.7)	<b>13</b>
<b>Drug consumption during pregnancy</b>							
No	16 (47.1)	5 (14.7)	2 (5.9)	2 (5.9)	4 (11.8)	5 (14.7)	<b>34</b>
Yes - analgesic	4 (66.7)	0 (0)	1 (16.7)	0 (0)	1 (16.7)	0 (0)	<b>6</b>
- antibiotic	1 (20)	2 (40)	0 (0)	0 (0)	1 (20)	1 (20)	<b>5</b>
- other	2 (40)	1 (20)	0 (0)	1 (20)	1 (20)	0 (0)	<b>5</b>
NTD - neural tube defect, FUO - fever of unknown origin							

Africa 1.7/1000,<sup>14</sup> Portugal 0.6/10000,<sup>15</sup> Germany 1.5/1000,<sup>16</sup> the north of England 17.9/10.000,<sup>17</sup> the north of France 10.94/10000,<sup>18</sup> and the USA 9.3-14.6/10000.<sup>19</sup> However, this rate is lower than China with 6/1000,<sup>20</sup> Turkey with 30.1/10000,<sup>21</sup> south-east of the Caspian Sea with 3.12/1000,<sup>22</sup> and north-east Iran with 50.1/10000.<sup>23</sup> Regarding gender, our results indicated that the rate of NTDs is higher in females than males, similar to rates reported by other researchers.<sup>19,23-27</sup> Among the NTD malformations, anencephaly was the most common, which was not similar in comparison with other studies.<sup>2,28</sup> Some reports have shown that spina-bifida is the most common form of NTD. The higher rates of NTDs we found when the conception took place in winter is in accordance with other investigations.<sup>22,23</sup> Some research has shown that parental consanguineous marriage is higher in NTDs.<sup>28,29</sup> In this study, 54% of parents had consanguineous marriages. Other investigations have shown that age is a complex risk factor in NTDs.<sup>30,31</sup> In some malformations, the rate of malformations is higher with increasing maternal age, but in NTDs, there is no linear relation between the high rate of NTDs and increasing maternal age. Meaning that mothers with age <18 and age >35, both have a high chance of newborns with NTDs.<sup>32-34</sup> In this study, 90% of mothers with NTD newborns did not consume folate before and during the first trimester of pregnancy. In recent years, extensive investigation has shown that folate has a preventive effect on NTDs.<sup>30,35-38</sup>

Concerning the high rate of NTDs in this region and due to multifactorial causes of NTDs, we conclude that folate deficiency, usage of drugs during pregnancy, and consanguineous marriage may play a role in predisposition to NTD. Therefore, further studies are essential.

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