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Prevalence of Neural Tube Defects in Yasuj, South West Iran

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Abstract

Background: Neural tube defects (NTDs), anencephaly, meningocele, and meningoencephalocele, are of the most common congenital anomalies of the central nervous system caused by defects in closure of the neural cord in the third and fourth gestational weeks. We aimed to investigate the prevalence of NTDs among the total births in clinics under supervision of Yasuj University of medical sciences, Yasuj, southwest Iran**.**

Methods: All newborns with NTDs who were delivered in obstetrics and gynecology hospital wards of Yasuj University of medical sciences, south west Iran, from April 2005 to March 2011 were included. The mothers with NTD deliveries were also compared with the mothers with physically healthy deliveries for blood indices. After an interview a form was filled regarding their demographic information such as maternal age, address, gestational age, mother's blood group, blood indices, and due date of delivery.

Results: Of the 14034 infants who were born in hospitals of Yasuj university of medical sciences, south west Iran, during the 6years period of this study, 68 (36 girls and 24 boys; P = 0.46) had NTDs. 59 (86.8%) infants had anencephaly and 9 (13.2%) had other types of NTDs. The prevalence of NTDs was 4.84/1000 birth during the 6years period. No significant difference was found between the groups regarding the other demographic variables and blood indices.

Conclusion: The prevalence of NTDs in Yasuj, is much higher compared with previous reports. This warning sign should be beard in mind by policy makers to address the related etiological factors and prevention plans.

Keywords: Neural tube defects; anencephaly; meningocele; meningoencephalocele; prevalence

Introduction

Neural tube defects (NTDs), including defects like anencephaly, meningocele, and meningoencephalocele, are of the most common congenital anomalies of the central nervous system caused by defects in closure of the neural cord in the third and fourth gestational weeks (1). These disorders can be prevented by up to 85% by the periconceptional use of 400 μg folic acid (2). The prevalence of NTD varies in different ethnic groups, with the highest prevalence reported in women of Hispanic ethnicity and the lowest prevalence in black and Asian women (3) (3, 4).

Some studies have been done on the prevalence of NTDs in some parts of the Islamic Republic of Iran. In a study on 8585 births in Hamadan (northwest Iran), this prevalence was 50.1/10000 (1991-1997) (5). In another study the prevalence of NTDs was 2.97/1000 in a sample of 16785 newborns (1997-2001) (6). Most of the reported cases of NTDs had a multifactorial etiology; in other words either genetics or environment played a role in the development of NTDs (7). Recent evidence suggests that several factors such as radiation, drugs, malnutrition, infections, seasonal changes, nitrated water, and genetics (such as mutations in folate-dependent pathways) may have adverse effects on normal development of the central nervous system since the time of conception (8) (1, 8, 9). NTDs might lead to miscarriage, still birth, fatality in early infancy, or disability during life time (10).

Improvement of health care services together with development in diagnostic methods and instruments has helped health care providers alleviate and control the prevalence of NTDs. Therefore, it is necessary to survey the prevalence of these defects in various areas and among different ethnicities in order to provide better healthcare services for more prevalent areas. We aimed to investigate the prevalence of NTDs among the total births in obstetrics and gynecology hospital wards of Yasuj University of medical sciences, southwest Iran, considering factors such as time, age distribution, and the patients' condition.

Patients and Methods

Primarily, In a descriptive standardized cross-sectional hospital-based study all newborns with NTDs (anencephaly, meningocele, and meningoencephalocele) who were delivered in obstetrics and gynecology hospital wards under supervision of Yasuj university of medical sciences, the main referral centers of the Kohgiluyeh and Boyer

Ahmad province which is covering an area of 15,563 square kilometers, mostly mountainous, with a population of about 634,000 (11), south west of Iran, from March 2005 to March 2011 were included to determine the prevalence of obvious NTDs and type of the NTD, and relationships with other demographic variables such as year of delivery, season and month as well as mother's age. Routine folic acid supplementation was prescribed to all of the mothers since 4 months before pregnancy.

In the next step, in a case-control study, the group of mothers with NTD deliveries (case group, n = 68) were compared with a group of randomly selected mothers with physically healthy newborns, group matched in number and birth date (control group, n = 68) considering variants such as blood group, hemoglobin concentration (Hb), white blood cell (WBC) counts.

Patients were usually from moderate to low socioeconomic class families of various ethnic backgrounds. The mothers in both groups were interviewed by a pediatrician and a form was filled by the interviewer regarding their demographic information such as maternal age, address, gestational age, mother's blood group, blood indices, and their due date of delivery. NTDs were defined according to the International Classification of Diseases, 10th Revision (ICD-10) and were confirmed by a pediatrician. Mothers who were admitted from locations other than Kohgiluyeh and Boyer Ahmad province were excluded. This study was approved by ethical committee of Yasuj university of Medical Sciences and informed written consent was obtained from both parents before enrolling the participants. Mothers had the permission to discontinue their participation during the study.

Data were analyzed using SPSS software (version 16.0). Analysis of variance (ANOVA) was used for comparing the case group with control group for Hb concentrations, blood group, and WBC counts. Chi-square and fisher's exact tests were used as appropriated for qualitative data.

Results

14034 infants were born during the 6 years period in Imam Sajjad hospital. Of them, 68 (4.84/1000 birth: 36 girls and 24 boys; P = 0.46) had NTDs, 4.84 in 1000 births. 59 (86.8%) infants had anencephaly and 9 (13.2%) had other types of NTDs. The distribution of NTDs is shown in tables 1 to 3 based on the year, season, and month of birth. Table 4 shows the maternal age-

specific prevalence of NTDs during the mentioned period. There were no data on maternal age of 20 women. 83.3% cases of NTDs occurred in 20-35 year-old mothers which are 5 times fewer than the mothers aged less than 20 years and higher than 35 year-old mothers. 22 women were in their first pregnancy, 24 women were in their second pregnancy, and 11 women had more than 2 pregnancies (missed cases = 11).

Maternal blood groups in the case group included: B^+ (7 women), O^+ (20 women), and A^+ (6 women). Other blood types were not detected in this group; however in the control group O^- and AB^+ were present. No significant difference was seen between the distribution of blood groups in the two groups (P = 0.385).

Data on Hb evaluation were available only for 33 mothers having neonates with NTDs and 26 mothers with normal neonates. There was no statistically significant difference (P = 0.553). No patient had white blood cell (WBC) counts less than 4500 (wbc / mcL). WBC counts were normal in 15 women and 13 women had WBC counts more than 12000 (wbc / mcL) which could be a sign of an infection or inflammation, but no significant difference was seen in this regard (P = 0.428).

Table 1. The Distribution of Obvious NTDs in Newborns of Yasuj from March 2005 to March 2011 by the Year of Delivery

Other types of NTD	Anencephaly	Prevalence of NTDs per 1000 births[a]	No. Obvious NTDs	No. of childbirths	Year
March2005-February2006	1722	8	4.6	100%	0
March 2006-February2007	2038	17	8.3	100%	0
March 2007-February2008	1871	11	5.9	82%	18%
March 2008-February2009	2305	8	3.5	100%	0
March2009-February 2010	2964	8	2.7	100%	0
March 2010-February2011	3134	16	5.1	56%	44%
Total	14034	68	4.84	87%	13%

[a] **P** = 0.16

Table 2. Seasonal Distribution of NTD Deliveries in Yasuj, Southwest Iran, from March 2005 to March 2011

Season	Number of childbirths	Prevalence of obvious NTDs	Prevalence of NTDs per 1000 births[a]	Anencephaly	Prevalence of other NTDs
Spring	3231	12	3.71	12	0
Summer	4010	16	3.99	12	4
Fall	3322	21	6.32	19	2
Winter	3471	19	5.47	16	3
Total	14034	68	4.84	59	9

[a] **P**=0.142

Table 3. Monthly Distribution of NTD Deliveries in Yasuj, Southwest Iran

Other types of NTD	Anencephaly	Prevalence of NTDs per 1000 births [a]	No. of obvious NTDs	No. of childbirths	*Month*
April	902	6	6.65	100%	0
May	1110	3	2.70	100%	0
June	1219	3	2.46	100%	0
July	1294	3	2.32	100%	0
August	1468	5	3.41	60%	40%
September	1248	8	6.41	75%	25%
October	1154	5	4.33	60%	40%
November	1096	8	7.30	100%	0
December	1072	8	7.46	100%	0
January	1279	8	6.25	100%	0
February	1220	2	1.64	100%	0
March	972	9	9.26	67%	33%
Total	14034	68	4.84	87%	13%

[a] P=0.09

Table 4. Maternal Age-Specific Prevalence of NTD Deliveries in Yasuj, Southwest Iran

No. other types of NTD(% of total)	No. of Anencephaly (% of total)	No. of obvious NTDs (% of total)	Maternal age
Less than 20	10 (14%)	8 (14%)	2 (15%)
20-30	36 (53%) [a]	27 (49%)	9 (69%)
31-35	14 (21%)	13 (24%)	1 (8%)
More than 35	8 (12%)	7 (13%)	1 (8%)
Total	68 (100%)	55 (100%)	13 (100%)

[a] **P = 0.073**

Discussion

In this study, the prevalence of NTDs in Yasuj was 4.84 per 1000 births be-

tween March 2005 and 2011 with the highest prevalence between 2006 and 2007 (8.34 per 1000 births) and the lowest between 2009 and 2010 (2.69 per 1000 births). Compared with other regions in the world and Iran, it was a relatively high prevalence. The prevalence of anencephaly was 4.2 per 1000 births and prevalence of other NTDs was 0.6 per 1000 births in this 6 years time period. In a study held in Yasuj in 1999, anencephaly and myelomeningocele ratios were 0.2 and 0.98 per 1000 births, respectively (12). A marked increase in this region was seen in contrast with the declining rate in the prevalence of NTDs in developed countries considering the fact that medical services, expert pediatricians, databases and registry systems were improved during this gap of time. Prevalence of NTDs in some other cities of Iran are as follows: Tehran: 1.76 per 1000 births (5), Khuzestan: 4.2 per 1,000 births (13), Birjand:2.97 per 1000 (6),Turkmen ethnicity:4.05 per 1000 births (14), native Fars ethnicity:2.52 per 1000 births (14), Sistani: 3.08 per 1000 births (14) Gorgan: 2.8 per 1000 (15), Zanjan: 6.2 per 1000 (16), and Sanandaj: 6.23 per 1000 (17). prevalence of NTD in some other countries are as follows: Poland: 2.6 per 1,000 births (18), Magdeburg, Germany: 1.64 per 1000 births (19) and Oman:1.25 per 1,000 births (20). Worldwide, prevalence of NTDs ranges from 1.4–2 per 1,000 live births (21). In the latter cities the prevalence ratios were higher than Yasuj. It doesn't seem that geographical distribution plays a part in occurrence of these defects. Further studies need to be done to compare these cities with respect to factors such as water, soil, humidity, weather, and socioeconomic status.

In Zanjan and Sanandaj cities of Iran, the prevalence ratio of anencephaly were 0.88 and 1.87, respectively which were lower than what was observed in Yasuj (16, 17). Golalipour and colleagues reported that spina bifida was the most common type of NTDs in the north of Iran (22). In Yasuj, anencephaly was the most common NTD by reaching the 86.8% of 4.84 cases of NTD per 1000 births which showed a high prevalence compared with reports from other regions (3, 4, 10, 23). Concerning other worldwide investigations, the prevalence of NTDs in North America was reported 2.5-3.5 per 1000 births and in northwest America was 0.21-0.3 per 1000 births (the lowest reported ratio); In England it was 2.8 per 1000 births (8). In some regions of neighboring countries such as Jeddah in Saudi Arabia, and Izmir in Turkey,

the prevalence of NTDs was 0.79 (23) and 1.5 per 1000 births (24), respectively, which were lower than many reported data in Iran as well as our observation in Yasuj. The current situation in Yasuj may be a warning sign for health care workers and policy makers.

We found that the prevalence of NTDs in 2006 was more than 2005. It was then decreased until 2010 and again there was a marked increase in 2010 which needs more investigations of causes and risk factors considering the fact that registry systems were more developed along with scientific developments of health care system. The prevalence was higher in autumn followed by winter. This could be because of the raise in viral diseases such as the flu; however, the difference was not statistically significant; it seems that pregnancies happening at the end of winter and the beginning of spring may have limitations to folic acid supplementation in the first months of pregnancy and it is probably due to unavailability of some kinds of fruits and vegetables sources of folic acid at these times. The highest prevalence of NTDs was in March (9.26) followed by December, November, April, September and January, respectively. The lowest ratio was in February (1.64) followed by May and June, respectively ($P = 0.656$).

Considering the age of pregnancy, the highest prevalence ratio of NTDs was 74% in 20-35 year-old mothers which is 5 times higher than mothers aged below 20 and over 35 years. No significant statistical difference was seen between various age groups ($P = 0.11$). This was inconsistent with another study reporting that possibility of NTDs in mothers aged below 20 and over 35 years was consequently higher (23). In this research, sex distribution of NTD prevalence was not even; affected girls were 1.5 times more than boys, which has also been reported in previous studies (12). According to the statistical analyses results there were no significant differences between the case group and the control group considering the blood type, WBC, and Hb concentrations. As a limitation of the present study, diagnosing the NTDs only by examination according to ICD-10 can be considered.

Our study included the essential data necessary for evaluating the prevalence of NTD in our region and is useful for other evaluation in this field as well as estimating the incidence and the prevalence of NTDs in a wider spectrum, and establishing a database for further investigations. However, more pro-

spective researches are needed to determine the factors involved in the prevalence of NTDs.

Overall, the prevalence of NTDs in Yasuj, south west of Iran, is much higher compared with other reports. This warning sign should be considered by policy makers to address the related etiological factors, For instance, nitrate ions concentration, as an effective factor in NTD occurrence (25), in tap water, which is revealed to be higher than standards according to reports from Yasuj university of medical sciences, and also intrafamiliar marriages which are highly occurred; these are also to be investigated for any influence on NTD prevalence in this area.

Conflicts of interest: No conflict of interest was reported.

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