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Original Article

Prevalence of Anencephaly in Gorgan, Northern Iran

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Background: Anencephaly is a neural tube defect incompatible with life. The aim of this prospective study was to determine the prevalence of anencephaly in Gorgan, northern Iran.

Patients and Methods: During 1998 – 2005, 49,534 newborns at Dezyani hospital in Gorgan were screened for neural tube defects. Clinical and demographic data of the diagnosed cases were recorded in a pre-designed questionnaire for analysis. These data included sex, ethnicity, parental consanguinity, and residential area.

Results: The overall prevalence of neural tube defects and anencephaly were 28 and 12 per 10000 births, respectively. The prevalence of anencephaly was 11 and 12 per 10000 births in male and female newborns, respectively. Considering the parental ethnicity, the prevalence of anencephaly was 12, 16, and 7 per 10000 in Fars, Turkman, and Sistani ethnicity, respectively. The prevalence of anencephaly was 13.1/10000 in newborns with mothers aged >35 years. Consanguinity was seen in 36% of the parents. The highest rate of anencephaly occurred in 1999 (23/10000) and the least was in 2003 (2/10000). The most prevalent season for the occurrence of anencephaly was winter (16/10000).

Conclusion: The present study indicated that the prevalence of anencephaly among Iranian newborns in northern Iran was higher than in the European population.

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Keywords: Anencephaly • birth defect • ethnicity • Iran • neural tube defects

Introduction

Birth defects are leading causes of pediatric hospital admissions, medical expenditures, and infant mortality. Neural tube defects (NTDs) are serious birth defects of the spine and brain. Two of the most common NTDs are spina bifida and anencephaly. Miscarriage, stillbirth, and a lifetime of disability are the outcomes of NTDs.

Anencephaly is a neural tube defect that is incompatible with life.[1] Risk factors for anencephaly are genetic, environmental, and maternal. Previous studies have suggested that there is a racial predilection for this condition.[2] Neural tube defects account for 21.7% of all notified congenital birth defects in Iran, with an incidence of 2.8 per 1000 live births in the period 1998 – 2005.[2] Our previous study has suggested that there might be an ethnicity difference in the incidence of NTD, with a higher predilection noted among the Turkman populations.[2] From 1993 to 2002, the overall incidence of anencephaly in Singapore was 0.58 per 1000 live births. The incidence was highest among the Malay population when compared with the Chinese population (P=0.03) and other races.[1]

Gorgan is the capital city of Golestan province in northern Iran, where different ethnicities such as native Fars, Turkman, and Sistani reside. The aim of this study was to determine the prevalence of anencephaly in addition to the demographic and maternal trend of this condition over an eight year period in this area.

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Materials and Methods

Data collection

We performed an analytic cross-sectional hospital-based study which included all live and stillborn newborns delivered in the Dezyani Teaching Hospital, Gorgan, from January 1998 until December 2005.

This hospital is the largest referral hospital in the city with an annual rate of more than 6000 deliveries that accounts for 80% of deliveries in the city and 20% of annual births in Golestan Province. Patients are usually from moderate to low socioeconomic class families of various ethnic backgrounds.

In Golestan Province, the three main ethnic groups are Fars, Turkman, and Sistani. The region has a population of about 1.8 million and covers an area of about 20,460 square kilometers.

NTDs were defined according to the International Classification of Diseases, Tenth Revision (ICD-10).[3] We aimed to estimate the prevalence of anencephaly in all ethnic groups and their relationship with maternal variables, associated malformations, prenatal diagnosis, and other demographic information. The design was based on a sample of 49,534 postpartum women after admission for delivery in maternity hospital in Gorgan.

Data were collected through interviews with mothers in the immediate postpartum period, as well as by reviewing the medical records of both the mothers and newborn infants.

Analysis

Data were analyzed by using SPSS software version 15 and STATA SE version 10 software and were compared with the Chi-square test. Because of the rarity of anencephaly, the 95% confidence interval for prevalence was estimated dependent upon the binomial exact method. A p value of 0.05 or less was considered statistically significant. All variables were included in the model a priori.

Results

During 1998 – 2005, there were 49,534 births (live and stillborn) at Dezyani Teaching Hospital, Gorgan. Of those, 56 and 138 newborns were diagnosed as having anencephaly and NTD, respectively. The prevalence of anencephaly during the eight year period was 12 per 10000 births. According to parental ethnicity, the prevalence rates of anencephaly were 12, 16, and 7 per 10000 amongst the Fars, Turkman, and Sistani ethnic groups, respectively. There were 27 male and 29 female newborns. The rate of anencephaly was 11 per 10000 and 12 per 10000 in male and female newborns, respectively. This difference was not significant.

Considering the mothers' age, the highest rate was 13.1 per 10,000 in newborns with mothers aged >35 years. Also the rate of anencephaly was 12.2 per 10,000 and 11.04 per 10,000 in newborns with mothers aged 15 – 19 and 20 – 34 years, respectively. These differences were not significant.

No associated congenital abnormalities were seen in 57.1% of the cases however there were 19.6% central nervous system, 8.9% musculoskeletal, 5.3% gastrointestinal, 3.5% head and neck, 1.7% heart, and 3.5% renal abnormalities. This study showed that 20 parents (36%) with affected newborns had consanguinity. Also 63% of the parents resided in rural areas and 38% in urban areas.

Figure 1 shows the rate of anencephaly for each year of the study period. The highest rate was in the year 1999 (23 per 10,000) and the least was in 2003 (2 per 10,000). The most prevalent season for occurrence of anencephaly was winter (16 per 10,000).

Discussion

In this study the prevalence of anencephaly during the eight year period was 12 per 10000 births. The prevalence of anencephaly was 104.4 per 10,000 births in China,[4] 0.5 – 0.6 per 1,000 in Singapore,[1] 0.01 to 7.42 per 10,000 in Rijeka, Croatia,[5] and 1.49/1,000 in Santos Dumont.[6]

In eastern Turkey, prior to the 1986 Chernobyl disaster, the prevalence of anencephaly was 1.7 per 1000, which was in contrast with the years after the disaster, when the prevalence of anencephaly was 5.5 per 1000. The increased rate reached a peak of 8.9 in 1988. In 1989 the rate decreased to 8.6 per 1000, and in 1990 the rate fell to 4.2 per 1000.[7]

Considering parental ethnicity, the prevalence rates of anencephaly were 12, 16, and 7 per 10000 in Fars, Turkman and Sistani, respectively in our study. The race-specific incidence of anencephaly was 7.6/10000 live births in the Malay population, higher than 5.5/10000 in the Chinese and

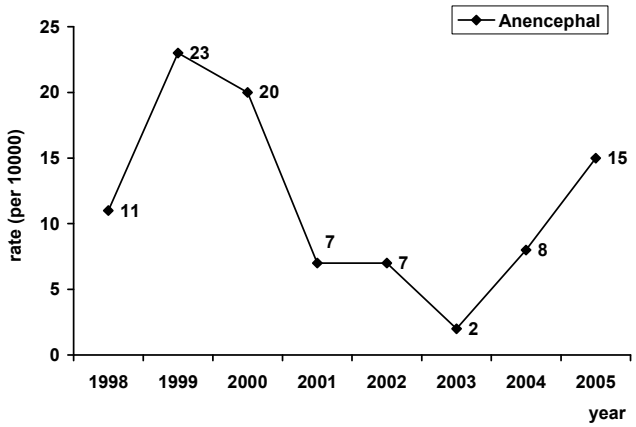

Figure 1. Annual rates of anencephaly (per 10 000 births) in Gorgan, Golestan Province, Iran, 1998 – 2005

5.0/10000 in the Indian population.[8] The prevalence of anencephaly was highest among Hispanic births, followed by non-Hispanic white births, with the lowest prevalence among non-Hispanic black births.[8] This difference in incidence rates both between and within races and ethnicities could possibly suggest the roles of dietary factors and a genetic predisposition for this condition, which warrants further study.

In our country a program for fortifying flour with folic acid in order to prevent neural tube defects began in 2006, thus we could not evaluate its benefits. However, there was a decline in anencephaly after starting the fortification program in South Africa,[9] USA, and Canada[10]. The rate also decreased in Singapore,[1] from 0.54/1000 in 1993 to 0.32/1000 in 2002. Significant declines in anencephaly were observed among Hispanic births and non-Hispanic white births after fortification.[8]

A high prenatal detection rate for anencephaly was reported by all registries; the highest efficiency (100%) was reported from the Czech Republic for anencephaly and encephalocele.[11] We suggest that obligatory reporting of all congenital malformations would be the first step toward this practice in Iran as well as in other developing countries. The importance of establishing national and international registries for congenital malformations in all countries is stressed.[5]

No associated congenital abnormalities were seen in 57.1% of our cases but 19.6% had CNS, 8.9% musculoskeletal, 5.3% gastrointestinal, 3.5% head and neck, 1.7% heart, and 3.5% renal abnormalities. Associated malformations were seen in 11.8% of infants with anencephaly in northeastern France (1979 – 2003),[12] and in 9.4% of infants in Singapore (1993 –2002). The latter malformations included: 29% gastrointestinal, 20% musculoskeletal, 11% CNS and amniotic band, 3% cardiac, renal and respiratory, and 20% other malformations.[1] In Rijeka, Croatia 81.8% anencephaly (1963 – 2000) was reported.[5]

The male prevalence of birth defects was 966.2 per 10000 births, which was significantly higher than the prevalence in females in China (2002 – 2004),[4] and Singapore (F:M=7:10, 1993 – 2002),[1] but the sex ratio in our study was F:M=29:27. In Rijeka, Croatia, it was 5:2[5] and in Brazil was 4:1.[6]

The highest rate of anencephaly was 13.1/10000 in newborns with mothers aged >35 years in our province but in Brazil the highest rate was observed in women aged 20 – 29 years (19 /10,000).[6]

The impact of folic acid fortification of flour for preventing neural tube defects in specific racial/ethnic groups has not been well described. Efforts to increase folic acid consumption for the prevention of NTDs in pregnancies among women of all races/ethnicities should be continued and studies to identify and elucidate other risk factors for NTDs are warranted.[8]

Maternal factors that are significantly associated with increased risk for anencephaly are: low education, maternal selective serotonin-reuptake inhibitors (SSRI) consumption, increasing gravidity or parity, history of previous miscarriages, positive history of birth defects, high or low age of mothers during pregnancy, increased stress of mothers, women employed in industry or agriculture, low socio-economic levels, maternal antipyretic consumption, and a low monthly income. The protective factors for anencephaly are

folic acid use, and multivitamin preparations. But no association was seen between paternal age and prevalence of anencephaly. Also no association with gestational pathology, exposition to high temperatures, mother's occupation, exposure to chemical or physical agents was found in other studies,[6] and no genetic or environmental factors were identified to account for a high incidence of anencephaly.[13]

Although no geographical factor was definitely identified, there has been a suspicion that the consumption of potatoes which have been infected by *Phytophotora infestans* at the beginning of pregnancy may have had an effect; but this hypothesis would have to be confirmed by microbiological studies.

Overall maternal factors associated with NTD were primary school education or lower, a history of a previous baby with a birth defect, history of a fever or cold, use of analgesic and antipyretic drugs, daily passive exposure to cigarette smoke, poor ventilation during heating and consumption of at least six meals per week containing pickled vegetables during pregnancy.[14]

The present study showed the high prevalence of anencephaly in Gorgan, a city in northern Iran. This study indicated that the prevalence of anencephaly among Iranian newborns in northern Iran was higher than in the European population.

Our findings will help establish a central registry system for future studies, which will focus on etiology, ethnic disparity, as well as environmental and nutritional factors of anencephaly in the south-east Caspian Sea region of the country.

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