



# Birth Prevalence of Neural Tube Defects in Iran: A Systematic Review

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## Abstract

**Context:** Neural tube defects (NTDs) are one of the most common birth defects with a high rate of mortality. Several studies have shown the reduction of the rate of NTD due to preconceptional usage and flour fortification with folic acid.

**Objectives:** The aim of this systematic literature review was to assess the appropriate information about the prevalence of Neural Tube Defects among the Iranian population, geographic areas of Iran.

**Data Sources:** We searched PubMed, Embase, Scopus, and data banks in Iran, such as the scientific information database (SID), Magiran, and Barekat knowledge network system from January 1969 to February 2017. The following keywords were used to search all fields in the above databases ("Neural Tube Defects" OR "NTD" AND "Iran").

**Study Selection:** NTDs were classified as given by Moore to include anencephaly, spina bifida, encephalocele, iniencephaly, and craniorachischisis. Primary outcomes of interest for estimating the prevalences were the total number of births (including live and stillbirths if available separately) and the total number of NTD affected births (including live and stillbirths if available separately).

**Data Extraction:** Data extracted from selected studies, included: first author, study design, city, sample size, duration of studies, and the prevalence of NTDs and subtypes of neural tube defects.

**Results:** A total of 429 studies were initially identified in the databases. After excluding duplicate studies, 244 articles were retrieved and reviewed based on their titles and abstracts; 221 articles were excluded. Twenty-three articles were selected for a more detailed review. There were some publications of the same study, data were extracted from the most complete and up-to-date publication. Four articles were added by reference searching and one forthcoming article was added. Finally, 21 articles have been included in the study.

**Conclusions:** The surveillance of NTD in Iran is currently limited due to the fact that provinces have established systems to report national and local NTD prevalence. However, when data are available, reported NTD prevalence, which varies by geographic region from 1.01 to 8.29 per 1000 live births, is in some areas of Iran.

**Keywords:** Neural Tube Defects, Prevalence, Iran

## 1. Context

Neural tube defects (NTDs) including encompassing spina bifida, anencephaly, and encephalocele are classified as a severe group of birth defects, which occurred during primary neurulation, three to four weeks after conception. Mortality, morbidity, and long-term disability and economic costs are related with NTDs (1, 2).

NTDs can be caused by multifactorial, genetic, and environmental factors. Some factors including maternal obesity, pre-gestational diabetes, and certain medicines such as anticonvulsants, folate deficiency during pregnancy, poor maternal nutrition, maternal ethnicity, infections, and seasonal changes can affect the rate of NTDs (2-4).

Registration or surveillance system of fetuses and infants screen the incidence rate of birth in developed coun-

tries. Indeed, international organizations have registration system to determine the surveillance and possible mechanism of causes of birth defects to establish prevention strategies in the world (5).

The incidence rates of NTD have reported 0.89 - 0.93 per 1000 during 1991 - 2011 in European countries (1), 0.53 per 1000 births in the USA during 1999 - 2007 (6), 0.2 to 9.6 per 1000 in Latin America during 1990 and 2010 (7), and 0.62 - 13.8 per 1000 in Arab countries (8).

## 2. Objectives

The aim of this systematic literature review was to assess the appropriate information about the prevalence of

Neural Tube Defects among the Iranian population, Geographic areas of Iran.

### 3. Data Sources

In this systematic review study, we reviewed the current literature regarding incidence and prevalence of neural tube defects. For this purpose, we searched PubMed, Embase, Scopus, and data banks in Iran, such as the scientific information database (SID), Magiran, and Barekat knowledge network system from January 1969 to January 2017. The following keywords were used to search all fields in the above databases (“Neural Tube Defects” OR “NTD” AND “Iran”). An addition, manual search was performed using reference lists from the research studies and review articles to identify other eligible studies.

### 4. Study Selection

NTDs were classified as given by Moore (9) to include anencephaly, spina bifida, encephalocele, Iniencephaly, and craniorachischisis. Primary outcomes of interest for estimating the prevalences were the total number of births (including live and stillbirths if available separately) and the total number of NTD affected births (including live and stillbirths if available separately). All titles and abstracts were initially screened for potential relevance and selected for further investigation if the outcomes of interest were identified by Mohammadi. Full-text articles potentially eligible for inclusion in this review were screened against the inclusion criteria independently and in duplicate by Mohammadi and Mobasheri. Any disagreements were resolved through discussion with a third reviewer, Golalipour.

### 5. Data Extraction

Data extracted from selected studies, included: first author, study design, city, sample size, duration of studies, the prevalence of NTDs, and subtypes of neural tube defects.

### 6. Results

A total of 429 studies were initially identified in the databases. After excluding duplicate studies, 244 articles were retrieved and we reviewed them based on their titles and abstracts. A total of 221 articles were excluded due to the following reasons: 150 irrelevant articles were excluded, 32 studies described risk factors for neural tube defects, and 9 articles did not report the number or

prevalence of neural tube defects among their outcomes. Twenty-five studies focused on non-human subjects and five studies provided data for folic acid fortification and prevalence of NTD (Figure 1).

Twenty-three articles were selected for a more detailed review; seven articles were excluded due to the overlapping period of studies. There were some publications of the same study, data were extracted from the most complete and up-to-date publication. Four articles were added by reference searching and one forthcoming article was added. Reviewed articles are summarized in Table 1.

### 7. Discussion

Prevalence of neural tube defects in Iran: Seventeen studies that reported on the prevalence of NTD among 676892 newborns were included (four studies sample size were not reported). The birth prevalence of NTDs reported ranged from 1.01 per 1000 total births to 8.29 per 1000 total births. All the studies included in the systematic review were hospital-based studies.

The incidence of neural tube defects in the study was highly variable (Figure 2). In Urmia (23), northwestern Iran, the rate of NTDs was the highest with 8.29 per 1000 births. Other studies that have been conducted in the western region of Iran have reported a high incidence rate, for example, Sanandaj (17) 6.23, Hamadan (12) 6.2, and Zanjan (21) 5.01.

The incidence of neural tube defects was based on six articles that were reported in the capital of Iran, Tehran (10, 12-14, 22, 28), between 1.01 to 3.8 per 1000 births, respectively.

In the city of Kashan, in central Iran (2), the incidence is almost the same and about two were reported.

Golalipour et al., reported that the incidence of neural tube defects in northern Iran was 1.01 (29), 2.8 (20), and 2.87 (19) per thousand births. The difference in the incidence of NTD may be due to increased maternal awareness of folic acid consumption and flour fortification of folic acid in the area.

In the only study conducted in Eastern Iran, Birjand, in 2006 by Afshar et al., (16), the incidence of neural tube defects has been reported 2.97.

As for the gender factor and the incidence of NTDs, among 14 studies, 10 studies reported females more than males (2, 12, 15, 16, 18, 19, 23-25, 28), the number of males was higher in two studies (13, 21), and in another two studies (17, 20) the incidence of neural tube defect in both sexes was almost equal.

In the Golalipour et al., study in 2007 (19), the NTD rates were 4.05/1000, 2.52/1000, and 3.08/1000 for mothers of

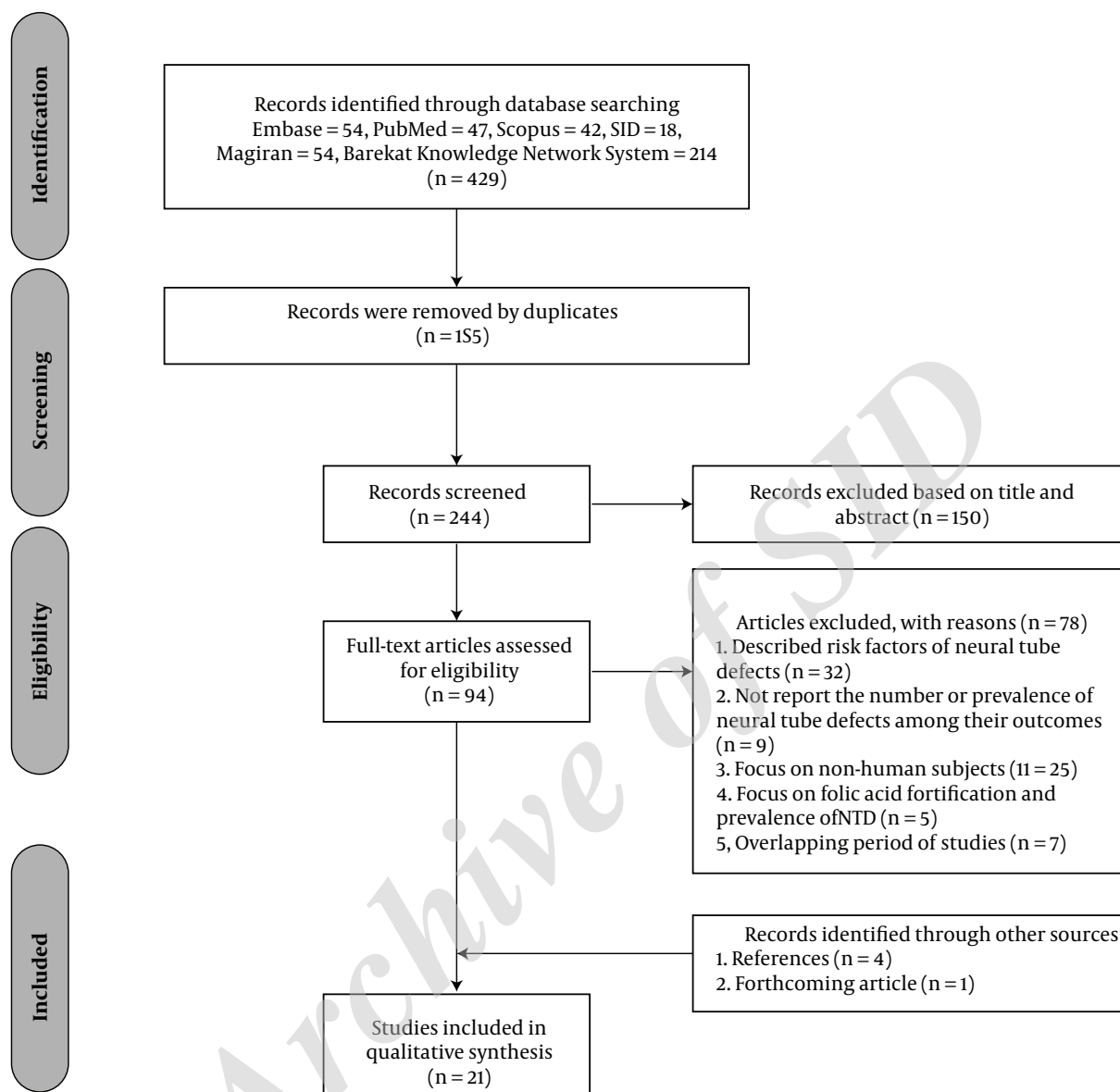


Figure 1. Flowchart of the studies selected for qualitative synthesis

Turkmen, native Fars, and Sistani ethnic groups, respectively (no significant difference).

As for the consanguinity marriage factor and the incidence of NTDs, among 7 studies, in the Afshar article (16), 27 (54%) of the 50 offspring were derived from consanguineous marriage; in the Behrooz study (25), as for the family relationship of the couple, 31% of women with pregnancies affected by NTDs were related to their husbands; Fakheri et al., (15), stated 13% of them had familial relationships; Gotalipour et al., in 2007 (19), showed 36 (33.0%) of the parents with affected newborns had consanguineous

marriages; Gotalipour et al., in 2010 (20), showed that 20 parents (36%) with affected newborns had consanguinity; Kesharvaz (25), stated 41.9% had a consanguinity relative with a spouse; and in the Talebian study (2), 26 (28.6%) of the 91 offspring were derived from consanguineous marriage.

To our knowledge, the present publication is the first one that reviews data on NTD prevalence in Iran, including time trends of NTD classification.

Our review study showed that 13 provinces reported NTD prevalence. Comparisons of NTD prevalence between

**Table 1.** Neural Tube Defects Prevalence Per 1000 Births by Province in Iran (21 Studies)

	Reference	Location	Study Duration	Total Births	Sample Size	Types of NTDs Evaluated	NTDs Prevalence Estimate Per 1,000
1	Farhud et al., 1986 (10)	Tehran	1969 - 1977	13,037	-	-	1.76
2	Farhud et al., 2000 (11)	Hamadan	1991 - 1997	8,585	-	1.56/1000 Anencephaly, 0.69/1000 Spina bifida	5.01
3	Zarkandi et al., 1995(12)	Tehran	Sep 1992 - Jul 1994	30,142	95	47 Anencephaly, 43 Myelomeningocele, 5 other	3.1
4	Safradian et al., 1999 (13)	Tehran	Mar1993 - Mar1998	28,449	67	27 Anencephaly, 18 Myelomeningocele, 4 Encephalocele, 1 Spina bifida hidden, 1 Anencephaly and Spina bifida, 1 Anencephaly and Myelomeningocele	2.4
5	Ketabchi et al., 2000 (14)	Tehran	Feb 1993 - Feb 1994	23,160	-	1.7/1000 Anencephaly, 1.4/1000 Spina bifida aperta, 0.26/1000 Encephalocele	-
6	Fakheri et al., 2005 (15)	Kermanshah	Mar 1996 - Mar2002	81,538	-	106 Anencephaly	1.3
7	Afshar et al., 2006 (16)	Birjand	Apr 1997 - Dec 2001	16,785	50	23 Anencephaly, 8 Spina bifida, 7 Spina bifida and hydrocephalus 6 NTD and other anomalies, 3 Encephalocele, 3 Iniencephaly	2.97
8	Mohammad Beigy et al., 2002 (17)	Sanandaj	Mar 1998 - Dec 2001	14,915	83	13 Anencephaly, 29 spina bifida, 14 myelomeningocele, 27 meningocele	6.23
9	Keshavarz et al., 2006 (18)	Shahroud	Mar 1998 - Sep 2002	14,588	42	18 Anencephaly, 18 spina bifida, 5 myelomeningocele, 1 meningocele	2.87
10	Golalipour et al., 2007 (19)	Gorgan	Jan 1998 - Dec 2003	37,951	109	62 spina bifida, 43 anencephalic, 4 encephalocele.	2.87
11	Golalipour et al., 2010 (20)	Gorgan	Jan1998 - Dec 2005	49,534	138	56 Anencephaly	2.8
12	Marzban et al., 2005 (21)	Zanjan	Mar 2001 - may 2002	2,250	14	5 myelomeningocele, 4 meningocele, 2 encephalocele, 2 Anencephaly, 1 myelomeningocele and Craniosynostosis	6.2
13	Eftekhari et al., 2008 (22)	Tehran	Mar 2001 - Mar 2004	38,473	143	54 Anencephaly, 47 myelomeningocele, 11 encephalocele, 9 spina bifida, 8 meningocele, 14 other	3.8
14	Abdi Rad et al., 2008 (23)	Urmia	Jan 2001 - Jun 2005	14,121	117	78 Anencephaly, 35 spina bifida, 4 encephalocele	8.29
15	Rouzitlab et al., 2013 (24)	Yasuj	Mar 2001 - Mar 2011	36,775	78	59 Anencephaly, 19 spina bifida	2.12
16	Behrooz et al., 2007 (25)	Ahvaz	Mar2002 - Mar 2004	13,262	56	30 Anencephaly, 15 spina bifida, 5 meningocele, 3 encephalocele, 3 Anencephaly and myelomeningocele	4.2
17	Ahmadzadeh et al., 2008 (26)	Ahvaz	Apr 2003 - Dec 2006	4,660	6	5 Meningocele and meningomyelocele, 1 Anencephaly	1.3
18	Sereshti et al., 2008 (27)	Shahrkord	Mar 2005 - Mar 2006	2,854	14	-	4.9
19	Delshad et al., 2009 (28)	Tehran	Mar 2005 - Mar 2007	61,112	62	52 Meningomyelocele, 10 Encephalocele	1.01
20	Talebian et al., 2015 (2)	Kashan	Feb 2007 - Dec 2012	38,936	91	72 spina bifida, 14 Anencephaly, 5 encephalocele	2.33
21	Mirfazeli et al. (29), (In Press)	Gorgan	Jan 2008 - Mar 2013	144,920	148	-	1.02

and within areas showed regional and/or local differences, most probably due to variations in data collection methods.

Briefly, in our study, clinical examination at birth in

hospitals was the main data collection methods used to estimate NTD prevalence. Geographic variation can be affected by the NTD prevalence.



Figure 2. Incidence of neural tube defects

## 8. Limitations

Lack of recording of legal and illegal termination of pregnancy with NTD can be affected by the NTD prevalence. Despite data limitations and geographic variation, these data are important due to the fact that they can show NTD prevalence changes over time.

## 9. Conclusion

The present publication is the first to review and report data on NTD prevalence in Iran including time trends of NTD classification. The surveillance of NTD in Iran is currently limited due to the fact that few provinces have established systems to report national and local NTD prevalence. However, when data are available, reported NTD prevalence, which varies by geographic region from 1.01 to 8.29 per 1000 live births, is located in some areas of Iran.

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