A national estimate of the birth prevalence of congenital anomalies in India: systematic review and meta-analysis

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Abstract

Background: A quarter of all global neonatal deaths occur in India. Congenital anomalies constitute the fifth largest cause of neonatal mortality in the country, but national estimates of the prevalence of these conditions are lacking. The objective of the study was to derive an estimate of the birth prevalence of congenital anomalies in India.

Methods: The search was carried out in PubMed and pooled prevalence was estimated using the inverse variance method. A random effects model was used due to high heterogeneity between the studies. Forest plots were generated using the Review Manager software.

Results: The PubMed search identified 878 articles from which 52 hospital based and three community based studies were included in the meta-analysis. The pooled prevalence of congenital anomaly affected births was 184.48 per 10,000 births (95% CI 164.74–204.21) among 802,658 births. Anomalies of the musculoskeletal system were highest among live births while the prevalence of central nervous system defects was highest when stillbirths were included in the analysis. Anencephaly and talipes were the most commonly reported anomalies.

Conclusions: Data from this meta-analysis suggests that there may be as many as 472,177 (421,652 to 522,676) congenital anomaly affected births in India each year. Population based studies using standard definitions are needed to validate these estimates. The two most frequently reported anomalies were anencephaly that is potentially preventable through preconception folate supplementation, and talipes which can be corrected using relatively low cost interventions. Studies are needed to determine the impact of congenital anomalies on neonatal mortality in India.

Keywords: Birth defects, Congenital anomalies, Congenital malformations, Birth prevalence, India, Meta-analysis

Background

A quarter of global neonatal deaths occur in India. In 2013, the country reported a neonatal mortality rate of 29 per 1000 live births, responsible for 753,000 neonatal deaths [1]. While the highest contributors to neonatal deaths were preterm births (34.7%), intrapartum complications (19.6%), pneumonia (16.3%) and neonatal sepsis (15%), congenital anomalies constituted the fifth largest cause, being responsible for an estimated 9% of neonatal deaths in the year 2010 [2]. There is evidence of transition in causes of infant and child mortality in low and middle-income countries, including India [3]. With a decrease in infectious causes of infant deaths, especially in urban areas in India, the proportion of mortality due to congenital anomalies is likely to increase [4]. Global estimates suggest that congenital anomalies affect 2–3% of births [5]. Assuming a 2% birth prevalence, and 25,595,000 births in 2013 [6], an estimated 511,900 births may have been affected with a congenital anomaly in India. These estimates exceed the combined totals of anomaly affected births occurring in several high-income countries [7]. The true magnitude of the number of births affected by congenital anomalies in India is unknown due to lack of a national birth defects surveillance. The need for data arises as currently there
is no data on the impact of congenital anomaly affected pregnancies or births on health service utilization, for either termination of pregnancy due to detection of a fetal anomaly or for neonatal intensive care services. Another requirement for data is to derive estimates of the number of children born with disabling conditions. Medical and rehabilitative services for affected children through government health services are currently limited in India, resulting in significant out of pocket expenditure for families [8, 9]. Data on the magnitude of congenital anomalies are also needed as some of these conditions can be prevented through primary care interventions targeted towards women in the preconception, intra-conception and antenatal periods [10]. Strategies targeting the prevention of births affected by congenital anomalies also target the shared risk factors for other adverse pregnancy outcomes, effectively aiming at reduction of reproductive wastage, and improving pregnancy outcome [11]. In this study, we systematically reviewed available Indian studies, in order to derive a national estimate of births affected by congenital anomalies in India. We also discuss the implications of this quantitative analysis in terms of prevention and care, further research needs, and the characteristics of a birth defects surveillance system in India.

**Methods**

**Search strategy**
A literature search was performed in PubMed in April 2015 using the keywords: (“congenital abnormalities”[MeSH Terms] OR (“congenital”[All Fields] AND “abnormalities”[All Fields])) OR “congenital abnormalities”[All Fields] OR (“congenital”[All Fields] AND “anomalies”[All Fields]) OR “congenital anomalies”[All Fields] AND (“epidemiology”[Subheading] OR “epidemiology”[All Fields] OR “prevalence”[All Fields] OR “prevalence”[MeSH Terms]) AND (“india”[MeSH Terms] OR “india”[All Fields])). No restrictions were used for date of publication. Further searches were carried out among the reference lists of eligible articles.

**Study selection**
All titles and abstracts identified in the PubMed search were screened for the possibility of extracting birth prevalence data. Studies were eligible to be included in the review if they fulfilled the following inclusion criteria: 1) reported data on the number of anomaly affected babies or anomalies identified at birth among either live born and/or stillborn babies and 2) were conducted in India. Exclusion criteria: 1) Case reports and papers focusing on etiology, diagnosis or clinical management were excluded. 2) Studies that reported prevalence data of only a single anomaly or system were not included in the analysis as these represented non-random, selected cases, and would therefore distort prevalence estimates.

**Data quality**
Studies were included if: 1) a clear description of study setting (hospital or community-based) was mentioned, 2) study reported total number of births in the given time period, and 3) number and type (live or stillbirth) of anomaly affected births amongst the total births was mentioned.

**Data extraction**
A data extraction form was designed in MS Excel for the following study characteristics: study and geographical setting, study duration, sample size, and primary outcomes of interest which included the number of anomaly affected babies or the number of anomalies and the number of births (live and stillbirths) as reported in the study. When a study was eligible for inclusion in the review, the numerator and denominator were verified and the prevalence estimate was recalculated.

**Statistical analysis**
Birth prevalence of congenital anomalies was calculated as the total number of babies (both live born and stillborn) with anomalies per 10,000 births [12]. The live birth prevalence was determined from the number of anomaly affected live births per 10,000 live births [12]. Pooled prevalence was estimated in Review Manager (version 5.3) software using the inverse variance method. Due to the high heterogeneity between studies ($I^2 > 95\%$, $p < 0.05$) the meta-analysis was conducted using a random-effects model.

**Results**

**Search results**
The PubMed search identified 878 articles, of which only 50 articles were identified to be of potential interest for inclusion in the review. A search of the reference lists of these 50 articles yielded a further 17 articles of potential interest, published in non-indexed Indian journals. Finally 54 articles fulfilled the inclusion criteria and were included in the review (Fig. 1).

**Study characteristics**
There were 52 hospital-based [13–63] and three community-based studies [64–66] (one article [58] reported two separate studies conducted in Mumbai (39,498 births) and Kolkata (19,191 births)). These 55 studies were reported between 1960 and 2015 (Table 1). Clinical examination was the major method of case ascertainment and was backed up only in 14 studies by radiological, ultrasound and other investigations [17, 20, 22, 23, 26–28, 33, 40, 48, 50–52, 60]. Nine studies
reported the involvement of neonatologists or pediatricians in case ascertainment [19, 26, 35, 39, 45, 49, 51, 62, 64]. The autopsy rate varied among the hospital studies ranging from 0 to 25% for stillbirths and early neonatal deaths. None of the studies reported the number of pregnancies terminated due to detection of fetal anomalies. Community studies were restricted to live births and did not report stillbirths and early neonatal deaths.

**Birth prevalence of congenital anomalies**

Data on births affected by congenital anomalies was reported from 52 hospital-based studies of which 47 studies reported both live and stillbirths while five studies reported only live births. The number of births screened ranged from 1000 to 141,540 for hospital-based studies. The reporting of anomalies was done during the period of hospital stay till discharge. The pooled prevalence of congenital anomaly affected births from 802,658 births using a random-effects model was 184.48 per 10,000 births (95% CI 164.74–204.21) (Fig. 2a). The five hospital-based studies reported a pooled live birth prevalence of 203.33 per 10,000 live births (95% CI 171.32–235.34) for 44,392 live births (Fig. 2b).

Community-based studies reported the prevalence of anomaly affected births within the first week post birth. The studies reported screening of live births ranging from 194 to 7590 live births. The pooled prevalence for community studies from 10,193 live births was 261.05 per 10,000 live births (95% CI 199.13–322.96) (Fig. 2c). Due to paucity of studies, analysis of congenital anomaly prevalence rates over time did not yield meaningful results.

**System-wise prevalence of anomalies**

Table 2 presents the system-wise prevalence of anomalies. Among hospital studies, which included data on both live births and stillbirths, anomalies of the central nervous system were most frequently reported, followed by anomalies of the musculoskeletal system (75.85 per 10,000 births (95% CI 58.80–92.90) and 65.64 per 10,000 births (95% CI 52.97–78.31), respectively). Cardiovascular system anomalies had the lowest birth prevalence across both hospital and community settings. Among
| Study                  | Study period | Study setting | Duration | Place          | Number of births | Number of anomaly affected births | Birth prevalence per 10,000 births |
|-----------------------|--------------|---------------|----------|----------------|------------------|----------------------------------|---------------------------------|
| Agarwal et al. 1991   | 1981–1984    | hospital      | 31.5 months | Lucknow       | 9405 births      | 192                              | 204.15                          |
| Agarwal et al. 2014   | 2010–2011    | hospital      | 12 months  | Bhubaneswar    | 7268 births      | 116                              | 159.6                           |
| Aiyar and Agarwal 1969| 1966–1967    | hospital      | 19 months  | Mumbai         | 10,000 live births | 172                              | 172²                           |
| Anand et al. 1988     | NM           | hospital      | NM        | Jamnagar       | 2000 births      | 40                               | 200                             |
| Bai et al. 1982       | NM           | hospital⁵     | 12 months  | Trivandrum     | 7167 births      | 132                              | 184.18                          |
| Bai et al. 1990       | NM           | hospital⁵     | 12 months  | Trivandrum     | 13,964 births    | 50                               | 35.81                           |
| Baruah et al. 2015    | 2010–2013    | hospital      | 34 months  | Dibrugarh      | 18,192 births    | 206                              | 113.24                          |
| Bharucha 1998         | 1993–1996    | hospital⁴     | 39 months  | Mumbai         | 42,304 births    | 972                              | 229.77                          |
| Bhat and Babu 1998    | 1989–1992    | hospital      | 40 months  | Pondicherry    | 12,797 births    | 353                              | 275.85                          |
| Chaturvedi and Banerjee1989| 1985–1986 | hospital⁵     | 12 months  | Wardha         | 3014 births      | 82                               | 272.06                          |
| Chinara and Singh 1982 | 1978–1979    | hospital⁴     | 12 months  | Varanasi       | 1774 births      | 37                               | 208.57                          |
| Choudhary et al. 1984 | 1976–1980    | hospital      | 60 months  | Kolkata        | 21,016 births    | 63                               | 29.98                           |
| Choudhary et al. 1989 | 1976–1987    | hospital      | 120 months | Kolkata        | 126,266 births   | 535                              | 42.37                           |
| Christopher and Jadhav1986 | 1979–1983    | hospital⁴     | 60 months  | Vellore        | 21,585 births    | 131                              | 60.69                           |
| Desai and Desai 2006  | NM           | hospital⁵     | 12 months  | Mumbai         | 2188 births      | 79                               | 361.06                          |
| Dutta and Chaturvedi 2000 | 1998–1999    | hospital⁴     | 13 months  | Wardha         | 2968 births      | 37                               | 124.66                          |
| Duttachoudhary and Pal1997 | 1991–1993    | hospital      | 36 months  | Durgapur       | 7242 births      | 26                               | 35.9                            |
| Ghosh et al. 1979     | 1974–1976    | hospital      | 29 months  | Kolkata        | 2019 births      | 29                               | 143.64                          |
| Ghosh et al. 1985     | 1969–1973    | community     | 40 months  | New Delhi      | 7590 live births | 189                              | 249.01⁴                         |
| Goravalingappa and Nashi1979 | 1986–1987    | hospital      | 15 months  | Hubli          | 2398 births      | 75                               | 312.76                          |
| Grover 2000           | 1991–1995    | hospital      | 60 months  | Shimla         | 10,100 births    | 180                              | 178.22                          |
| Hemrajani et al. 1971 | 1965–1969    | hospital⁴     | 60 months  | Jaipur         | 28,511 births    | 608                              | 213.25                          |
| JaiKrishan et al. 1999| 1995–1998    | hospital      | 41 months  | Kerala         | 36,805 births    | 538                              | 146.18                          |
| JaiKrishan et al. 2013| 1995–2011    | hospital      | 191 months | Kerala         | 141,540 births   | 1370                             | 96.79                           |
| Joseph et al. 2010    | 2004–2005    | community     | 6 months   | Belgaum        | 194 live births  | 4                                | 206.19⁴                         |
| Khanna and Prasad 1967| 1964         | hospital      | 9 months   | Patna          | 5376 births      | 74                               | 137.65                          |
| Kolah et al. 1967     | 1960–1963    | hospital      | 39 months  | Mumbai         | 23,568 births    | 331                              | 140.44                          |
| Kulkarni et al. 1987  | 1984         | hospital      | 6 months   | Davangere      | 2000 births      | 81                               | 405                             |
| Kulshetra et al. 1983 | 1976–1977    | community     | 24 months  | Ballabhgarh    | 2409 live births | 79                               | 327.94⁴                         |
| Manwah et al. 2014    | 2010–2011    | hospital      | 12 months  | Patiala        | 1554 births      | 69                               | 444.02                          |
| Mathur et al. 1975    | 1970         | hospital⁴     | 4 months   | Hyderabad      | 1060 births      | 33                               | 311.32                          |
| Mishra and Baveja 1989| 1983–1987    | hospital      | 48 months  | Allahabad      | 4098 births      | 60                               | 146.41                          |
| Mital and Grewal 1969 | 1967–1968    | hospital      | 15 months  | Kanpur         | 4150 births      | 93                               | 224.1                           |
| Modi et al. 1998      | 1993–1997    | hospital      | 40 months  | Baroda         | 31,775 births    | 651                              | 204.88                          |
| Parmar et al. 2010    | 2006–2007    | hospital      | 18 months  | Bhavnagar      | 4210 births      | 37                               | 87.89                           |
| Patel and Adhia 2005  | NM           | hospital      | 24 months  | Mumbai         | 17,653 births    | 294                              | 166.54                          |
live births, anomalies of the musculoskeletal system were highest in both hospital (79.38 per 10,000 live births (95% CI 32.32–126.44)) and community settings (65.88 per 10,000 live births (95% CI 23.13–108.63)). The corresponding prevalence of central nervous system defects was lower (28.93 per 10,000 live births (95% CI 13.64–44.22) for hospital-based studies and (26.19 per 10,000 live births (95% CI 15.55–36.83) for community-based studies).

**Prevalence of selected anomalies**

Table 3 presents pooled prevalence of certain frequently reported congenital anomalies among hospital studies. Anencephaly was the most commonly reported anomaly with a birth prevalence of 21.1 per 10,000 births (95% CI 16.91–25.29) followed by talipes (birth prevalence 17.9 per 10,000 births (95% CI 15.09–20.71)), orofacial clefts (birth prevalence 14.94 per 10,000 births (95% CI 12.64–17.24)) and hypospadias (birth prevalence 12.20 per 10,000 births (95% CI 9.79–14.60)) among the 25 studies examining all births occurring in the hospital. Among hospital studies that excluded stillbirth data, the pooled prevalence of talipes (35.08 per 10,000 live births, 95% CI 16.88–53.29) was higher than anencephaly (17.11 per 10,000 live births, 95% CI 13.59–20.63) among live births.

**Discussion**

Congenital anomalies are not prioritized as public health problems in low income countries as they are considered to be rare conditions that are self-limiting due to the high mortality of affected infants [67]. Another reason for under-prioritization of these conditions is the understanding that most birth defects are not preventable through low-cost primary care strategies, the major approach of public health services of low income countries. In this study, we derived a national estimate of the birth prevalence of congenital anomalies occurring in India, as such data are currently unavailable due to lack of birth defects surveillance. Using a systematic literature search followed by meta-analysis, we derived a pooled prevalence of congenital anomaly affected births of 184.48 per
10,000 births (95% CI 164.74–204.21). This prevalence is slightly lower than that reported by the European Surveillance of Congenital Anomalies registry (215.54 affected births per 10,000 births (95% CI 214.14–216.94)) [68]. In terms of absolute numbers, however, these estimates indicate that congenital anomalies are not rare events in India, as the data suggests that between 421,652 to 522,676 anomaly affected births may be occurring in the country each year. Due to the reporting of stillbirths in hospital-based studies, anencephaly was the most frequently reported anomaly, followed by talipes, orofacial clefts and hypospadias. Neural tube defects (NTDs) like anencephaly are potentially preventable through a low cost primary prevention method of pre-conception folic acid supplementation [69, 70], but there are as yet no national guidelines on folic acid fortification/supplementation in India. Combined with pre-conception iron supplementation, this primary care intervention could not only reduce the number of NTDs in the country, but also reduce anemia, a persistent maternal health challenge in low income countries [71]. Community-based studies reported a higher prevalence of musculoskeletal anomalies, with talipes, a potentially treatable anomaly, being reported as the most common congenital anomaly among live births. Thus, in addition to determining the large numbers of affected births, this review identified that the two most commonly reported congenital anomalies were preventable/treatable through low cost methods. For example, the management of talipes through casting is relatively inexpensive, is widely available, and with proper compliance will prevent disability.

Our estimates however have to be considered as best-available data, as there was high heterogeneity among the studies, also reported in previous meta-analysis on NTDs in India [72, 73]. Due to the time-period included in the analyses, the definitions of anomalies varied, although the system-wise categorization of major anomalies was not too deviant from the International Classification of Diseases Version 10 (ICD-10) classifications. Stratified analysis over time did not yield any meaningful trends. It is noteworthy that institutional deliveries were only 26% in 1992–93 [74], but progressed to 79% in 2015–16 [75]. Birth defects data from studies conducted during the earlier period could be influenced by the high number of home births, and this could also be a limitation in the estimates. Most of the studies were hospital based. Community based studies were few, and none of the studies mentioned data on home births. For hospital based studies, the catchment areas of hospitals are undetermined due to high patient mobility. Furthermore, the studies included data from large public hospitals which frequently serve as referral centers for high risk mothers and complicated cases. Such methodological issues could be one of the reasons for the different rates observed for anencephaly versus spina bifida, as the latter is the more common condition [68]. Another factor influencing the estimates was that majority of the studies used only clinical assessment for case ascertainment. Incomplete ascertainment may therefore contribute to under-estimation of some anomalies. For example, the low prevalence of congenital heart defects as compared to available registry data could be ascribed to use of only physical examination at the time of birth [68]. Similarly, Down syndrome which is one of the most common birth defects, was not reported in most of the included studies. This discrepancy could be because our meta-analysis included studies that reported birth defects detected in the first week of life, while Down syndrome may be diagnosed after discharge. Another very important source of under-estimation would be the lack of data on termination of pregnancies due to fetal anomaly, as none of the studies reported this data. It should also be pointed out here that only PubMed was used for search of articles, and there may be a possibility that some articles were missed.

Despite these limitations, this review is important, as it is the first to report the magnitude of birth defects in India, and the need to establish a systematic method of surveillance for these conditions. The first point arising from the study is to determine whether surveillance for birth defects in India should be hospital or population based [12]. Data from a network of hospitals forms the cornerstone of existing birth defects registries in developed nations. Apart from systematic data collection, all deliveries occur at hospitals in these settings, and the populations accessing these hospitals are more or less well defined. In contrast, hospital based data will be inappropriate for India due to a number of reasons. Firstly, presence of large numbers of private hospitals would make inclusion of all in the reporting network difficult, leading to a risk of under-estimation of the number of cases. Till date, data reporting is not mandatory from private hospitals in India. Inappropriate inclusion of a major referral hospital, or a hospital providing free services into a birth defects surveillance network could also mislead estimates. Furthermore, unlike the well demarcated populations catered to by hospitals in developed countries, the population catered to by hospitals in India are extremely heterogeneous. There is significant patient mobility, as most healthcare is choice based, and financed through personal expenditure. The hospitals could cater to maternity cases from any part of the country, and these could include mothers from rural or urban areas. Cultural practices, such as preferred delivery at maternal residence could also confound results on geographic distribution of birth defects. All these factors highlight that hospital based surveillance could yield poor quality data, and may even misguide health services...
Fig. 2 Pooled prevalence of congenital anomalies. a. pooled prevalence of congenital anomaly affected births (both live and stillbirths) in hospital setting. b. pooled prevalence of congenital anomaly affected live births (hospital setting). c. pooled prevalence of congenital anomaly affected live births (community setting)
by suggesting occurrence of clustering of cases due to improper selection of hospitals into the reporting network.

Under such circumstances, true data on birth defects can be obtained from population-based birth defects surveillance, with active surveillance from carefully selected populations, identified in different parts of the country. One of the major functions of birth defects registries is to monitor maternal exposures, such as the prevalence of micronutrient deficiencies, poor maternal health status, agricultural lifestyles or other occupational exposures. India has several high risk situations and areas. Industrial catastrophes like the Bhopal gas tragedy or reports of children with severe birth defects in areas where banned pesticides are being used are examples of populations where communities can be selected, and long term surveillance can be initiated. Many of the risk exposures are shared for several other adverse pregnancy outcomes. Thus, surveillance for birth defects will be an added asset to monitoring maternal and child health outcomes in the country. In addition to selection of population based sites for surveillance, there is the need for adopting standardized definitions and methodology for case ascertainment. Inclusion of data on elective terminations of pregnancy after detection of fetal anomalies and follow-up of infants to include anomalies detected at later ages are important considerations when planning surveillance to reduce under estimation. For countries with limited resources the recently published manual for birth defects surveillance is an excellent tool that enlists steps for facilitating birth defects surveillance [12]. Use of such tools and population based surveillance will permit comparison of data on birth defects in low income countries with those reported from existing congenital anomaly registries.

Conclusions

In conclusion, this meta-analysis identified that as many as 472,177 (421,652 to 522,676) births affected by congenital anomalies may be occurring in India each year, with anencephaly and talipes being the most frequently reported anomalies. The high reporting of anencephaly suggests the need for a preconception folic acid supplementation programme, but nation-wide studies on implementation have to be conducted. The occurrence of talipes and other anomalies requiring surgical correction suggests the need to strengthen referral services for treatment/management of children born with birth defects. In terms of public health implications, the meta-analysis was unable to identify data on the impact of congenital anomalies on neonatal mortality. The impact of congenital anomalies on childhood disability was however apparent as both anencephaly and talipes are potentially disabling conditions. The analysis identified the need for future studies using standard definitions and methodology so that the data would be globally comparable. In terms of hospital versus population based surveillance, the analysis suggested the need for establishing population based registries with active surveillance for birth defects and maternal risk exposures from carefully selected populations.

Table 2 Pooled prevalence of anomalies by affected systems

| System                      | Birth prevalence per 10,000 births (n = 14 hospital studies) | Live birth prevalence per 10,000 live births (n = 3 hospital studies) | Live birth prevalence per 10,000 live births (n = 3 community studies) |
|-----------------------------|---------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------|
| Central nervous system      | 75.85 (95% CI 58.80–92.90)                                   | 28.93 (95% CI 13.64–44.22)                                         | 26.19 (95% CI 15.55–36.83)                                          |
| Musculoskeletal system      | 66.64 (95% CI 52.97–78.31)                                   | 79.38 (95% CI 32.32–126.44)                                        | 65.88 (95% CI 23.13–108.63)                                        |
| Cardiovascular system       | 27.06 (95% CI 20.03–34.09)                                   | 23.04 (95% CI 4.69–41.39)                                         | 9.32 (95% CI -0.81 – 19.45)                                        |
| Gastrointestinal system     | 50.19 (95% CI 42.50–57.87)                                   | 37.72 (95% CI 26.41–49.03)                                        | a                                                                   |
| Genitourinary system        | 39.08 (95% CI 27.86–50.30)                                   | 28.41 (95% CI 16.18–40.65)                                        | 37.42 (95% CI 13.14–61.70)                                        |

*Data not analyzed due to misclassification of umbilical hernia as gastrointestinal system anomalies.

Table 3 Pooled prevalence of selected anomalies

| Anomaly             | Birth prevalence per 10,000 births (n = 25 hospital studies) | Live birth prevalence per 10,000 live births (n = 5 hospital studies) |
|---------------------|-------------------------------------------------------------|---------------------------------------------------------------------|
| Anencephaly         | 21.10 (95% CI 16.91–25.29)                                  | 17.11 (95% CI 13.59–20.63)                                          |
| Exomphalos / omphalocele | 4.65 (95% CI 3.23–6.07)                                   | 1.60 (95% CI 0.46–2.74)                                             |
| Gastrochisis        | 7.00 (95% CI 4.56–18.56)                                   | 1.60 (95% CI 1.60–1.60)                                             |
| Hypospadias         | 12.20 (95% CI 9.79–14.60)                                  | 5.39 (95% CI 3.19–7.59)                                             |
| Orofacial clefts    | 14.94 (95% CI 12.64–17.24)                                  | 15.69 (95% CI 11.74–19.63)                                         |
| Spina bifida        | 5.85 (95% CI 4.48–7.21)                                    | 8.45 (95% CI 3.08–13.81)                                           |
| Talipes             | 17.90 (95% CI 15.09–20.71)                                  | 35.08 (95% CI 16.88–53.29)                                         |
Abbreviations
CI: Confidence Interval; MV: Not mentioned; NTDs: Neural tube defects

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Authors’ contributions
PB conducted the literature review, data analyses and drafting of the manuscript. AK conceptualized the study, reviewed the search and selection of articles and analyses of the data and contributed in writing the final manuscript. Both authors have read and agree on the final version of the manuscript.

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Not applicable.

Competing interests
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