Burden and consequence of birth defects in Nepal—evidence from prospective observational study

Prajwal Paudel  
Ministry of Health and Population Nepal

Avinash K Sunny  
Golden Community

Rejina Gurung  
Golden Community

Abhishek Gurung  
Golden Community

Honey Malla  
Golden Community

Netra B Rana  
Ministry of Health and Population Nepal

Nawaraj KC  
Ministry of Health and Population Nepal

Ashish KC (✉️ ashish.k.c@kbh.uu.se)  
Uppsala Universitet

Ram Narayan Chaudhary  
Ministry of Health and Population Nepal

Research article

Keywords: birth defects, Nepal, prevalence, risk factor, mortality

DOI: https://doi.org/10.21203/rs.3.rs-41322/v1

License: 🎓 This work is licensed under a Creative Commons Attribution 4.0 International License.  
Read Full License
Abstract

**Background**—Every year an estimated 7.9 million babies are born with birth defects. Of these, more than 3 million die and a further 3.2 million suffer from a disability. In order to address this, countries require data to enable better resource allocation for prevention, management and rehabilitation of babies born with birth defects. This paper contributes to this evidence base, assessing the prevalence of birth defects, associated risk factors and health consequences in Nepal.

**Method**—This is a prospective observational study conducted in 12 hospitals in Nepal for 18 months. All the women who delivered in the hospitals during the study period were enrolled. Independent researchers collected social and demographic data using semi-structured questionnaires at the time of discharge. Clinical events and birth outcome information were extracted from clinical case notes. Data were analysed to determine the prevalence and type of birth defect. Logistic regression was performed to assess risk factors and health outcomes of babies born with a birth defect.

**Results**—Among the total 87,242 livebirths, the prevalence of birth defects was found to be 5.8 per 1000 live births. The most common birth defects observed were anencephaly (3.95%), cleft lip (2.77%), cleft lip and palate (6.13%), clubfeet (3.95%), eye abnormalities (3.95%) and meningomyelocele (3.36%). The odds of having a baby with a birth defect was higher for mothers younger than 20 years (adjusted Odds ratio (aOR) 1.64; 95% CI, 1.18-2.28) and those from disadvantaged ethnicity (aOR 1.78; 95% CI, 1.46-2.18). The odds of birth asphyxia was almost double for babies with birth defect (aOR 1.88; 95% CI, 1.41-2.51) when compared to babies without a birth defect. The odds of neonatal infection was nearly double for babies with birth defect (aOR 1.82; 95% CI, 1.12-2.96) compared to babies without a defect. Babies with a birth defect had three-fold risk of pre-discharge mortality (aOR 3.00; 95% CI, 1.93-4.69).

**Conclusion**—Babies with birth defect have a higher risk of birth asphyxia, neonatal infection and pre-discharge mortality at birth. A portion of birth defect could have been prevented through micro-nutrient supplementation, a portion can be managed through surgery and rehabilitation.

**Funding**—Swedish Research Council (VR)

**Introduction**

Birth defects are anomalies in morphogenesis during early foetal life resulting in structural, behavioural, functional and metabolic disorders that can be detected prenatally, at birth or later in infancy [1]. Globally, more than 3 million babies with birth defects die within the first 28 days of life and a many survivors suffer from disabilities [2, 3]. Lower- and middle-income countries (LMICs) carry the greatest burden (90%) of birth defects globally, which are often least prioritized compared to other causes of neonatal and infant mortality for prevention and management [2, 3]. Some disorders, such as congenital heart disease and neural tube defects, carry a high risk of mortality [2, 4]. [5], In Nepal, each year an estimated 40,000 babies are born with a birth defect, among which cleft lip and palate, neural tube defects, and congenital heart disease rank as the most common conditions [6, 7]. Often, these factors are recognised
as genetic in origin (10-30%), environmental (5-10%), multi-factorial (20-35%) and unknown (30-45%) [8]. These factors may play a role during a critical period of development occurring in the first trimester when the baby is undergoing crucial stages of formation starting from fertilization, implantation and organ formation [1, 8]. There are several factors that can increase the risk of birth defects including maternal age, lack of nutritious diet, non-use of peri-conceptional folic acid, alcohol and tobacco consumption, exposure to pesticides and X Rays, and infection. These risk factors can be discussed with mothers during counselling and screening through effective antenatal care (ANC) [9, 10]. Therapy, medication, surgery, or assistive technology are further interventions for prevention and management of birth defects. In most cases, essential paediatric surgery can avert early mortality and long-term disability [11]. [12]. Prenatal diagnostic techniques, genetic counselling, and access to termination of pregnancy for foetal abnormality are examples of interventions to support women and reduce some neonatal mortality and still birth [13].

In LMICs, lack of diagnostic and national screening programmes has resulted in the paucity of nationally representative data, resulting in a major hurdle for in-depth understanding of the epidemiology of birth defects [14]. In Nepal, no national protocol regarding management and timely service provision for babies born with birth defects exists. To further accelerate the reduction of neonatal mortality rate to achieve the Sustainable Development Goals (SDG) target of 12 per 1000 live birth, it is critical to implement evidence-based interventions to prevent and manage birth defects [15, 16]. This study will provide evidence on the prevalence, risk factors and health outcomes associated with birth defects across 12 hospitals in Nepal.

Method

Study design and setting

This paper presents data from a prospective observational study conducted in 12 public hospitals across Nepal to evaluate the efficacy of a scale up of Helping Babies Breathe Quality Improvement Project implemented from 1 July 2017 to 17 October 2018 [17]. The hospitals were selected from different geographic locations across the country. All the hospitals were referral level public hospitals with more than 1000 deliveries per year.

Study participants

All babies born in the 12 hospitals during the study period were selected for this study. Only liveborn babies were included for analysis. Stillborn babies, out-born babies, and babies whose mothers did not consent to participate in the study were excluded from the study.

Data collection and management

In the selected hospitals, a data surveillance system was established for collection of data on the mothers and newborns. Obstetric data were collected through patient files and the maternity register in the maternity wards using a data retrieval form (additional file 1). Socio-demographic data were collected
through face-to-face interviews with mothers before discharge. Data coordinators assessed the forms for completeness, which was then indexed, sealed and sent to the head office for further action. In the central office, the data management team, led by a data manager, sorted, indexed, filed and reassessed forms for completeness. Data entry operators entered the indexed forms based on the hospitals in Census and Survey Processing System (CSPro). The data was cleaned and exported to the Statistical Package for the Social Sciences (SPSS) for further data analysis.

**Variables in the study**

Liveborn babies with birth defects were the variable of interest for this study. Demographic variables included age of mother, ethnicity, maternal literacy, type of fuel used for cooking in household and smoking habit. Antenatal variables included ANC check-up by doctor/nurse, parity of mothers and severe anemia during pregnancy. Intrapartum variables included mode of delivery, multiple deliveries, sex of the baby and weight of the baby at birth.

Demographic characteristics were categorized as age- less than 20 years, 20-34 years and 35 and above; ethnicity- relatively advantaged and relative disadvantaged group;

Obstetric characteristic, parity was categorized as 0 previous birth, 1 previous birth and 2 or more previous birth;

Birth asphyxia was defined as apgar score less than 6 at 1 minute;

Low birth weight was defined as birth weight less than 2500 gram;

Neonatal infection was defined as newborns with signs of clinical infection or positive septic screening with birth weight 1500 gram or more and/or gestational age 32 weeks or more;

Pre-discharge mortality included deaths of newborn with birth defects before discharge.

**Statistical analysis**

Prevalence of birth defects was calculated based on the total number of congenital cases reported and total number of live births in the same period. Cross-tabulation was performed for socio-demographic, obstetric and neonatal characteristics. Binary logistic regression was performed to analyse the level of association between the background characteristics and birth defects. The significance was determined at p<0.05. All variables with p<0.2 in the univariate analysis were considered for multi-variate logistic regression analysis.

**Ethical consideration**

All mothers provided written consent prior to the start of data collection. Confidentiality of data was maintained. Ethical approval was received from the Ethical Review Board of Nepal Health Research Council (reference number 26-2017).
Results

Out of the total 104,223 admissions, 87,989 deliveries occurred during the study period. Of these, 87,242 deliveries were live births and 747 deliveries were stillbirths. Among the livebirths, there were 506 cases of birth defects (Figure 1). The prevalence of birth defects was found to be 5.8 per 1000 live births. The different types of birth defects as reported from the data show that the more common disorders recorded were anencephaly (3.95%), cleft lip (2.77%), cleft and palate (6.13%), clubfeet (3.95%), eye abnormalities (3.95%) and meningomyelocele (3.36%). Most (75.89%) of the reported cases have not been classified (Figure 2).

Univariate analysis showed significant association with birth defects for most of the socio-demographic, obstetric and neonatal characteristics. Socio-demographic characteristics such as ethnicity and type of fuel used for cooking in the household showed significant association (<0.001) with birth defects. Female child was significantly associated with birth defects (p=0.002). Women with one previous birth (p=0.002), two or more previous births (<0.001), and having multiple delivery (p=0.02) were significantly associated with birth defects. The socio-demographic, obstetric and neonatal characteristics which were different in birth defect and reference group were considered for multi-variate analysis (Table 1).

Multivariate analysis revealed several factors which had a significant association with birth defects. Mothers less than 20 years of age were 1.64 times more likely (aOR 1.64; 95% CI, 1.18-2.28, p-value=0.003) to have a birth defects compared to mothers 20-<35 years of age. Mothers of relatively disadvantaged ethnic group were 1.78 times more likely (aOR 1.78; 95% CI, 1.46-2.18, p value=<0.001) to have babies with birth defects than relatively advantaged group. Female babies had a 1.35 times higher risk (aOR 1.35; 95% CI, 1.13-1.61, p value <0.001) of having birth defects compared to male babies. Compared to women with no previous birth, the risk of birth defect was 1.58 times higher among women with 1 previous birth (aOR 1.58; 95% CI, 1.26-1.98; p<0.001) and 2.33 times higher compared to women with 2 or more previous births (aOR 2.33; 95% CI, 1.84-2.95; p<0.001). Further, mothers with multiple deliveries had 1.8 times the risk of having babies with a birth defect compared to mothers with single deliveries (aOR 1.8; 95% CI, 0.98-3.28; p=0.06) (Table 2).

When considering health outcomes, the multi-variable analysis showed that babies with birth defect were 1.88 times higher risk of birth asphyxia (aOR 1.88; 95% CI, 1.41-2.51; p<0.001) compared to babies without a birth defect. Babies with a birth defect also had 1.82 higher risk of neonatal infection (aOR 1.82; 95% CI, 1.12-2.96; p<0.02). The risk of pre-discharge mortality for babies with birth defects was 3.31 times higher (cOR 3.31; 95% CI, 2.13-5.14; p<0.001) compared to babies without any birth defects (Table 3).

Discussion

The prevalence of birth defects in the present study is 0.58%, which is comparable to other studies in Nepal, Iraq and Iran which reported an incidence of 0.69% and 0.36% [18–20]. Our study showed that
Musculoskeletal System to be most commonly affected, presenting as cleft lip, cleft palate and club feet which is in line with studies reported from Egypt and India [21, 22]. A study in Iran and India reported higher prevalence of malformations from CNS, Cardiovascular system or Gastrointestinal system [23, 24]. This variation in patterns could possibly be explained by various genetic and environmental factors interplaying differently in varied time and geographical location [10].

Mothers younger than 20 years old were found to have a higher risk of delivering a newborn with birth defect, which is similar to the study which concluded association between young mothers and congenital anomaly [25]. Young women in Nepal are at higher risk of micro-nutrient deficiency, mal nourishment due to poor diet. These might have attributed to birth defect [25].

According to different literatures, congenital malformation is seen in multiple pregnancy rather than singleton pregnancy [10, 26]. Likewise, our finding enlisted this study as one among those many. However, multiple delivery did not pose a risk to birth defect in Europe [27]. Alterations of the blood flow within the vascular anastomoses supplying the twins and early primary abnormality that might develop during twinning itself can lead to birth defects [28]. Early antenatal care check to detect multiple birth and early screening of birth defect is critical.

In comparison to women with no previous birth, the likelihood of giving birth to a baby with congenital defect was seen among women with 1 or more previous birth in our study, which is similar to those reported in other studies [25, 29]. The decrement in body nutrients stores among mothers who have previously delivered as compared to those who have never delivered a baby before explains the association between parity and congenital birth defects [30]. Women in Nepal have micro-nutrient deficiency and poor nutrition status, more than one birth will deplete the micro-nutrient store [31].

With regards to ethnicity, advantageous ethnic groups were comparatively less likely to be associated with birth defects than the non-advantageous group. Association of ethnicity with birth defects has been depicted in the previously done studies [25, 32]. Ethnic variance as the risk for malformations may be linked to genetic susceptiveness or to socio-cultural and economic differences that might modify exposures [33]. Further, studies have shown that women from relatively disadvantaged group have poor nutrition and chronic micro-nutrient deficiency [33]. Also, women from these group have less access to antenatal care service for early screening of high risk pregnancy.

Babies with birth defects tend to have morbidities such as birth asphyxia and neonatal infection. The risk of mortality among these babies at birth is higher than babies without birth defect.

**Strengths and Limitations**

There are several strengths and limitations in this study. A community-based study can better project prevalence of birth defects. In our settings, echocardiography and other advanced diagnostics were not routinely available to diagnose malformations, which may lead to underrepresentation of disorders [21]. Stillbirths were not included in the study which might also have attributed to the lower prevalence. Further,
many birth defects, such as congenital heart defects, are not diagnosed at birth and so the overall prevalence may be underreported.

**Conclusion**

The prevalence of birth defects across the study population was 0.58% among newborn babies. Various socio-demographic factors, like age and disadvantaged ethnic group, are associated with birth defects. Obstetric factors such as number of previous birth are associated with birth defect. Babies with birth defects have higher risk for birth asphyxia, neonatal infection and pre-discharge mortality at birth. There is a need to improve the services available for babies with birth defect for better identification and management of these babies. These findings also urges for setting up a system of birth defect surveillance in hospitals such that special care and tracking can be done for better outcome.

**Declarations**

*Ethics Approval and Consent to Participate*

The ethical approval for the study was taken from the Ethical Review Board (ERB) of Nepal Health Research Council (reg. no. 26-2017). Written consent was obtained from the participants enrolled in the study.

*Consent to publish*: Not applicable

*Availability of data and materials*: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

*Competing interest*: None

*Funding*: Swedish Research Council (VR), Sweden. The funders had no role in design of the study.

*Authors’ contribution*

AKC, PP and AG conceptualized the study. AG and AKS conducted the first draft of the analysis. AKC reviewed the statistical analysis. PP and AKS made the first draft. RG, HM, NR, NKC, RNC, AKC reviewed and revised the manuscript. All authors read and approved the final version of the manuscript.

*Acknowledgement*: We would like to acknowledge and thank our database manager, Omkar Basnet in the data analysis and cleaning. Research team members and all the mothers who consented to the study. We would like to thank Nisso Nurova for reviewing the manuscript.

**Abbreviations**

LMIC- Low and Middle Income Countries, HIC- High Income Countries, SNCU- Sick newborn care unit
References

1. Blackburn ST: Maternal, Fetal, & Neonatal Physiology: A Clinical Perspective. Third edition: Saunders Elsevier; 2007.

2. Higashi H, Barendregt JJ, Kassebaum NJ, Weiser TG, Bickler SW, Vos T: The burden of selected congenital anomalies amenable to surgery in low and middle-income regions: cleft lip and palate, congenital heart anomalies and neural tube defects. Arch Dis Child 2015, 100(3):233-238.

3. World Health Organization: WHO Facts sheet on Congenital Anomalies. In. Geneva; 2016.

4. Ndibazza J, Lule S, Nampijja M, Mpairwe H, Oduru G, Kiggundu M, Akello M, Muhangi L, Elliott AM: A description of congenital anomalies among infants in Entebbe, Uganda. Birth Defects Res A Clin Mol Teratol 2011, 91(9):857-861.

5. World Health Organization SEARO: Birth defects in South-East Asia: a public health challenge: situation analysis. In. New Delhi; 2013.

6. World Health Organization SEARO: South East Asia Regional Neonatal-Perinatal Database. In. New Delhi; 2010.

7. Malla BK: One Year Review Study of Congenital Anatomical Malformation at Birth in Maternity Hospital (Prasutigriha), Thapathali, Kathmandu. Kathmandu Univ Med J (KUMJ) 2007, 5(4):557-560.

8. Zhu H, Kartiko S, Finnell RH: Importance of gene-environment interactions in the etiology of selected birth defects. Clin Genet 2009, 75(5):409-423.

9. Queisser-Luft A, Stolz G, Wiesel A, Schlaefer K, Spranger J: Malformations in newborn: results based on 30,940 infants and fetuses from the Mainz congenital birth defect monitoring system (1990-1998). Arch Gynecol Obstet 2002, 266(3):163-167.

10. Shawky RM, Sadik DI: The role of genomics in prevention or reducing the impact of congenital malformations. Genet Couns 2011, 22(2):135-141.

11. Sitkin NA, Ozgediz D, Donkor P, Farmer DL: Congenital anomalies in low- and middle-income countries: the unborn child of global surgery. World J Surg 2015, 39(1):36-40.

12. Warf BC, Alkire BC, Bhai S, Hughes C, Schiff SJ, Vincent JR, Meara JG: Costs and benefits of neurosurgical intervention for infant hydrocephalus in sub-Saharan Africa. J Neurosurg Pediatr 2011, 8(5):509-521.

13. Mohammad Jafar Golalipour, Mousa Ahmadpour-Kacho, Vakili Ma: Congenital malformations at a referral hospital in Gorgan, Islamic Republic of Iran. Eastern Mediterranean Health Journal 2005, 11(4):707-715.

14. Nacul L, Moorthie S, Kapila M, Zimmern R: Addressing congenital causes of disability. Lancet 2010, 375(9712):374.

15. Kc A, Jha AK, Shrestha MP, Zhou H, Gurung A, Thapa J, Budhathoki SS: Trends for Neonatal Deaths in Nepal (2001-2016) to Project Progress Towards the SDG Target in 2030, and Risk Factor Analyses to Focus Action. Matern Child Health J 2020, 24(Suppl 1):5-14.
16. Ministry of Health and Population N: Nepal's Every Newborn Action Plan 2016-2030. In. Kathmandu; 2016.

17. Kc A, Ewald U, Basnet O, Gurung A, Pyakuryal SN, Jha BK, Bergstrom A, Eriksson L, Paudel P, Karki S et al: Effect of a scaled-up neonatal resuscitation quality improvement package on intrapartum-related mortality in Nepal: A stepped-wedge cluster randomized controlled trial. PLoS Med 2019, 16(9):e1002900.

18. Taboo ZA-A: Prevalence and Risk Factors for Congenital Anomalies in Mosul City. Iraqi Academic Scientific Journal 2012, 11(4):458-470.

19. Ameen SK, Alalaf SK, Shabila NP: Pattern of congenital anomalies at birth and their correlations with maternal characteristics in the maternity teaching hospital, Erbil city, Iraq. BMC Pregnancy Childbirth 2018, 18(1):501.

20. Mashhadi Abdolahi H, Kargar Maher MH, Afsharnia F, Dastgiri S: Prevalence of congenital anomalies: a community-based study in the northwest of Iran. ISRN Pediatr 2014, 2014:920940.

21. Sarkar S, Patra C, Dasgupta MK, Naye K, Karmakar PR: Prevalence of congenital anomalies in neonates and associated risk factors in a tertiary care hospital in eastern India. J Clin Neonatol 2013, 2(3):131-134.

22. Mohamed A. El Koumi EAAB, Ibrahim Lebda: Pattern of congenital anomalies in newborn: a hospital-based study. Pediatric Report 2013, 5(1).

23. F. Khatami GAM: Survey of congenital major malformation in 10,000 newborns. Iranian Journal of Pediatrics 2005, 15(4).

24. Suguna Bai NS, Mascarene M, Syamalan K, Nair PM: An etiological study of congenital malformation in the newborn. Indian Pediatr 1982, 19(12):1003-1007.

25. Croen LA, Shaw GM: Young maternal age and congenital malformations: a population-based study. Am J Public Health 1995, 85(5):710-713.

26. Chen CJ, Wang CJ, Yu MW, Lee TK: Perinatal mortality and prevalence of major congenital malformations of twins in Taipei city. Acta Genet Med Gemellol (Roma) 1992, 41(2-3):197-203.

27. D. Căpățînă. CGC: Risk factors associated with congenital anomalies in children. ARS Medica Tomitana 2015, 2(21).

28. Pharoah POD: Causal Hypothesis for Some Congenital Anomalies. Twin Res Hum Genet 2005, 8(6):543-550.

29. Perveen F, Tyyab S: Frequency and pattern of distribution of congenital anomalies in the newborn and associated maternal risk factors. J Coll Physicians Surg Pak 2007, 17(6):340-343.

30. Hernandez-Diaz S, Werler MM, Walker AM, Mitchell AA: Folic acid antagonists during pregnancy and the risk of birth defects. N Engl J Med 2000, 343(22):1608-1614.

31. Budhathoki SS, Bhandari A, Gurung R, Gurung A, Kc A: Stunting Among Under 5-Year-Olds in Nepal: Trends and Risk Factors. Matern Child Health J 2020, 24(Suppl 1):39-47.
32. Egbe A, Lee S, Ho D, Uppu S: **Effect of Race on the Prevalence of Congenital Malformations among Newborns in the United States.** *Ethn Dis* 2015, **25**(2):226-231.

33. Egbe A, Uppu S, Lee S, Stroustrup A, Ho D, Srivastava S: **Congenital malformations in the newborn population: a population study and analysis of the effect of sex and prematurity.** *Pediatr Neonatol* 2015, **56**(1):25-30.

**Tables**

**Table 1. Socio-demographic, obstetric and neonatal characteristics**
| Variables | Birth defect | No Birth defect | Total | p-value | OR (95% CI) |
|-----------|--------------|-----------------|-------|---------|--------------|
| **Age of mother (n=87112)** | | | | | |
| 0-<35 years | 442(87.4%) | 77722(89.7%) | 78164(89.7%) | 0.15 | 1.25(0.93-1.69) |
| 20 years | 47(9.3%) | 6604(7.6%) | 6651(7.6%) | <0.001 | 1.84(1.51-2.25) |
| 35 years | 17(3.4%) | 2280(2.6%) | 2297(2.6%) | 0.28 | 1.31(0.81-2.13) |
| **Literacy (n=66949)** | | | | | |
| literate | 19(6.0%) | 3063(4.6%) | 3082(4.6%) | 0.249 | 1.31(0.83-2.1) |
| illiterate | 300(94.0%) | 63567(95.4%) | 63867(95.4%) | | |
| **Ethnicity (n=87112)** | | | | | |
| Relatively advantaged ethnic group | 131(25.9%) | 33897(39.1%) | 34057(39.1%) | | |
| Relatively disadvantaged ethnic group | 375(74.1%) | 52709(60.9%) | 53147(60.9%) | <0.001 | 1.84(1.51-2.25) |
| **Smoking (n=66949)** | | | | | |
| No | 297(93.1%) | 60869(91.4%) | 61166(91.4%) | | |
| Yes | 22(6.9%) | 5761(8.6%) | 5783(8.6%) | 0.268 | 0.78(0.51-1.21) |
| **Sex of the baby (n=87112)** | | | | | |
| Boy | 239(47.2%) | 46836(54.1%) | 47129(54.0%) | 0.002 | 1.32(1.10-1.57) |
| Girl | 267(52.8%) | 39770(45.9%) | 40037(46.0%) | | |
| **Parity (n=87101)** | | | | | |
| No previous birth | 172(34.1%) | 39882(46.1%) | 40054(46.0%) | | |
| Previous birth | 183(36.2%) | 30472(35.2%) | 30655(35.2%) | 0.002 | 1.39(1.13-1.72) |
| or more previous birth | 150(29.7%) | 16242(18.8%) | 16392(18.8%) | | |
| **antenatal check up (n=66949)** | | | | | |
| Yes | 316(99.1%) | 66015(99.1%) | 66331(99.1%) | | |
| No | 3(0.9%) | 615(0.9%) | 618(0.9%) | 0.974 | 1.02(0.33-3.19) |
| **time for first ANC check up (n=66331)** | | | | | |
| First trimester | 189(59.8%) | 29594(44.8%) | 29783(44.9%) | 0.008 | 1.68(1.15-2.46) |
| Second trimester | 96(30.4%) | 28276(42.8%) | 28372(42.8%) | 0.58 | 0.89(0.59-1.34) |
| Third trimester | 31(9.8%) | 8145(12.3%) | 8176(12.3%) | | |
| **Severe anemia during pregnancy (n=6002)** | | | | | |
| No | 28(96.6%) | 5804(97.2%) | 5832(97.2%) | | |
| Yes | 1(3.4%) | 169(2.8%) | 170(2.8%) | 0.841 | 1.23(0.17-9.07) |
| **Multiple delivery (n=87112)** | | | | | |
| No | 495(97.8%) | 85667(98.9%) | 86162(98.9%) | | |
| Yes | 11(2.2%) | 939(1.1%) | 950(1.1%) | 0.02 | 2.03(1.11-3.69) |
Table 2. Multivariate analysis of risk factors associated with Birth defects (n=66123)

| Age of mother | p-value | aOR(95% C.I.) |
|---------------|---------|---------------|
| 20-<35 years  | Reference |               |
| <20 years     | 0.003   | 1.64(1.18-2.28) |
| >35 years     | 0.79    | 0.94(0.57-1.54) |

| Ethnicity     | p-value | aOR(95% C.I.) |
|---------------|---------|---------------|
| Relatively advantaged ethnic group | Reference |               |
| Relatively disadvantaged ethnic group | <0.001  | 1.78(1.46-2.18) |

| Sex of the baby | p-value | aOR(95% C.I.) |
|-----------------|---------|---------------|
| Boy             | Reference |               |
| Girl            | 0.001   | 1.35(1.13-1.61) |

| Parity          | p-value | aOR(95% C.I.) |
|-----------------|---------|---------------|
| No previous birth | Reference |               |
| 1 previous birth | <0.001  | 1.58(1.26-1.98) |
| 2 or more previous birth | <0.001  | 2.33(1.84-2.95) |

| Multiple delivery | p-value | aOR(95% C.I.) |
|-------------------|---------|---------------|
| No                | Reference |               |
| Yes               | 0.06    | 1.80(0.98-3.28) |

| Constant | p-value | aOR(95% C.I.) |
|----------|---------|---------------|
|          | 0.001   | 0.002         |

Table 3. Consequences among babies with birth defects

| Variables                  | Birth defect | No Birth defect | p-value | cOR (95% CI) | p-value | aOR (95% CI) |
|----------------------------|--------------|-----------------|---------|--------------|---------|--------------|
| Low birth weight           | 99(0.7%)     | Ref             | 0.18    | 1.17(0.93-1.45) | 0.23    | 1.15(0.92-1.44) |
| (n=14676)                  |              |                 |         |              |         |              |
| Birth asphyxia             | 53(1.1%)     | Ref             | <0.001  | 1.94(1.46-2.59) | <0.001  | 1.88(1.41-2.51) |
| (n=4971)                   |              |                 |         |              |         |              |
| Neonatal infection         | 17(1.2%)     | Ref             | 0.004   | 2.05(1.26-3.33) | 0.02    | 1.82(1.12-2.96) |
| (n=1462)                   |              |                 |         |              |         |              |
| Pre-discharge mortality    | 21(1.8%)     | Ref             | <0.001  | 3.31(2.13-5.14) | <0.001  | 3.00(1.93-4.69) |
| (n=1149)                   |              |                 |         |              |         |              |

*adjusted with age of mother, sex of the baby, parity and multiple delivery

Figures
Figure 1

Participants flow figure
Figure 2

Types of birth defects (n=506)