Original article

Prevalence and associated factors of birth defects among newborns at referral hospitals in Northwest Ethiopia

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Abstract

Background: A birth defect is a structural or functional abnormality observed in children. Birth defects occur during intrauterine development of embryo or fetus. Birth defects may be visible before birth, at birth or later in life, and are major causes of children's hospital admissions and deaths.

Objectives: The aim of this study was to assess the prevalence and identify the associated risk factors of birth defects.

Method: A retrospective cross-sectional study was conducted in two referral hospitals where 19,650 infants were born between 2015 and 2017. Among these, 317 infants born with birth defects were selected, and the types of birth defect were identified. To identify associated risk factors, 321 maternal medical history books were selected by simple random sampling. The data were collected using a semi-structured checklist.

Results: A total of 19,650 infants were delivered during the study period. Among these, 1.61% of the infants had birth defects. The most frequent types of birth defect were neural tube defects (32.5%), followed by oro-facial clefts (27.1%), cardiovascular system defects (12%) and upper and lower limb defects (8.8%). Lack of folic acid supplementation (95% CI: 3.54-12.08), presence of chronic disease (95% CI: 2.27-7.21), intake of drugs (95% CI: 1.98-6.38) and consumption of alcohol during pregnancy (95% CI: 1.13-3.60) were significantly associated with birth defects.

Conclusion: The study identified a high prevalence of birth defects in infants born in Northwest Ethiopia. The most frequent type of birth defect was neural tube defect. In addition, the absence of maternal folic acid supplementation and the presence of chronic diseases during pregnancy were among the risk factors significantly associated with birth defects. Further detailed, nationwide, multicenter, retrospective/prospective follow up investigations should be conducted to influence political and healthcare decision-making so as to reduce birth defects. [*Ethiop. J. Health Dev.* 2018;32(3):00-000]

Key words: Birth defects, prevalence, associated factors

Introduction

Developmental disorders during delivery are described using different terms, such as birth defects (BDs), congenital malformation and anatomic abnormalities (1). A birth defect can be defined as an absence of structures and functions that normally form during the development of the embryo. It may be recognized prenatally, during delivery or in postnatal developments. The clinical conditions associated with BDs are usually observable during delivery. The frequent types of birth defect are congenital heart disease (CHD), neural tube defects (NTDs), oro-facial clefts (OFCs) and upper and lower limb defects (2, 3).

In early human history, birth defects in both animals and humans were often attributed to a curse from God or because of evil. Even today, some cultures think that mothers who give birth to infants with BDs have had communication with a devil or evil spirits (4).

Birth defects usually begin during organogenesis (from the 3rd to the 8th embryonic periods) (5). The cause of birth defects are not yet well known (1). However, the etiologies of birth defects are thought to be multifactorial inheritance, environmental teratogens, micronutrient deficiencies, chromosomal disorders and single gene defects. In developing countries, maternal infectious disease, such as rubella and syphilis, are purported to be common causes of birth defects (6).

Globally, the prevalence of major birth defects was 4% to 6%. Among these, 2% to 3% are diagnosed in live-born infants, and 2% to 3% are manifested in children around 5 years old (5).

Worldwide, permanent disability and death of children are the results of the undesirable effects of birth defects. Annually, around 3.3 million children below the age of 5 die of birth defects. In addition, 303,000 infants die within a month of being born because of birth defects, and 3.2 million live-born children are disabled for life, which has a direct impact on children, family, health care systems and communities (7).

In both developed and developing countries, although BDs are the most serious cause of infant mortality and disability, about 94% of BDs, 95% of deaths and 15-30% of hospital admissions of infants and children due to BDs are in low and middle income countries (8). One previously conducted prevalence study in Northwest Ethiopia, which included one of the hospitals in the present study, reported that the

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prevalence of BDs was 1.9% (9). This indicates there is a relatively high prevalence of BDs in this geographical region of Ethiopia.

The main aim of this study was to estimate the prevalence of BDs and to identify associated risk factors among newborn infants in two referral hospitals in Northwest Ethiopia, as there was very little data available, especially on associated factors. Moreover, a high level of prevalence of BDs was reported in the earlier study mentioned above, and the results from the current study would give an insight into the magnitude of the problem and provide baseline data for future detailed studies. In addition, information from this study would be useful in developing strategies for the prevention of birth defects as well as for improved management and rehabilitation of patients with BDs.

Materials and methods

Method of data collection: The type of study was an institution-based, retrospective, cross-sectional study. The study was conducted in two governmental referral hospitals: Debre Markos referral hospital (DMRH) and Felege Hiwot referral hospital (FHRH), in East and West Gojjam zones of Amhara region, Ethiopia. These hospitals were selected based on patient load. Also, they are the only referral hospitals in the East and West Gojjam zones of Amhara region.

Data collectors were selected in each of the two governmental hospitals, and they were trained for two days regarding the objectives of the study, about inclusion and exclusion criteria, and on sampling procedures. All 19,650 infants born between 2015 and 2017 were included in the study. To identify the associated risk factors of BDs, a total of 346 computer-generated samples were taken by simple random sampling from the total number of infants born. However, only 321 infants were included in the study based on the completeness of the data. Among these, 104 infants were born with BDs and 217 infants were born with no BDs. Data were also collected on socio-demographic and clinical information.

Data were collected from hospital records between October 2017 and January 2018. In order to determine the magnitude of BDs and the associated risk factors, all 19,650 infants' medical records were reviewed. The infants born with BDs were selected from a list containing the total number of infants born. The types of BD were identified based on maternal medical registration books. The data in medical history record books were collected by using a pre-tested semi-structured checklist. The checklist included: maternal socio-demographic characteristics (age, occupation and residency), general features of infant (sex), type of BD, and the associated risk factors of BDs (maternal history of folic acid supplementation, maternal history of alcohol consumption, maternal history of disease and maternal history of drug use).

The data were collected from delivery wards and neonatal intensive care units (NICUs) by the assigned data collectors (midwives) working at the study hospitals. Gynecologists/obstetricians and pediatricians were consulted when there was an ambiguous diagnosis. The proportions of children with BDs were calculated by dividing the number of birth BD cases (numerator) by the total number of live and stillborn infants (denominator).

Data processing and analysis: After checking for completeness, the data were entered into Epi-data version 3.1 and exported to SPSS version 24 for analysis.

Descriptive statistics, such as frequency distribution, percentages and tables, were used to describe the socio-demographic variables, the percentage of types of BD and the percentage of types of NTD.

Bivariate followed by multivariable logistic regression analyses were carried out to determine factors associated with BDs. The 95% confidence interval was determined and a p-value less than 0.05 were considered as statistically significant in all of the analyses.

Ethical consideration: Ethical clearance was secured, prior to data collection, from the Departmental Research Ethics Review Committee (DRERC) of the Department of Bio-Medical Sciences, School of Medicine, Debre Markos University and from the Institute of Review Board (IRB) of the School of Medicine, College of Health Sciences, Addis Ababa University. The anonymity of the patients and confidentiality of the data were maintained by the investigator and research assistants throughout the study.

Results

Prevalence of birth defects: In DMRH and FHRH, a total of 19,650 infants were born during the study period. In the context of our study, the study period is the 'data collection period' (October 2017 to January 2018). Of the 19,650 infants, 317 (1.61%) had BDs. The proportion of male infants who had BDs was greater than that of female infants. The majority of infants with BDs were rural residents (55.2%), followed by urban residents (44.8%) (Table 1).

Table 1: **The socio-demographic characteristics of study subjects in FHRH* and DMRH***, 2018**

Variables		FHRH		DMRH		Total	
		number	%	number	%	number	%
Gender	Male	86	46.0	101	54.0	187	59.0
	Female	77	59.2	53	40.8	130	41.0
Age	<35 years	58	55.2	47	44.8	105	33.1
	≥35 years	105	49.5	107	50.5	212	66.9
Residence	Urban	72	50.7	70	49.3	142	44.8
	Rural	91	52.0	84	48.0	175	55.2
Occupation	Farmer	88	50.9	85	49.1	173	54.6
	Government employee	24	49.0	25	51.0	49	15.4
	Private employee	38	55.9	30	44.1	68	21.5
	Unspecified	13	48.1	14	51.9	27	8.5

*FHRH = Felege Hiwot referral hospital; **DMRH = Debre Markos referral hospital

Types of birth defects: Among the 317 infants diagnosed with BDs, the most frequent types of BD were neural tube defects (NTDs) (32.5%), followed by oro-facial clefts (OFCs) (27.1%), cardiovascular system defects (CVSDs) (12%), upper and lower limb defects (8.8%), digestive and abdominal wall defects (6.6%), unspecified congenital malformation (5.4%), Down syndrome (3.2%), genitourinary system defects (2.8%) and head, face and neck defects (1.6%) (Table 2).

Table 2: **The frequency distribution of BD by sex from 2015-2017 in FHRH and DMRH, 2018**

Variables	Male number (n=187)	%	Female number (n=130)	%	Total number (n=317)	%
Neural tube defects	59	31.6	44	33.8	103	32.5
Oro-facial clefts	51	27.3	35	26.9	86	27.1
Cardiovascular system defects	22	11.8	16	12.3	38	12.0
Upper and lower limb defects	19	10.2	9	6.9	28	8.8
Digestive and abdominal wall defects	13	7.0	8	6.2	21	6.6
Unspecified congenital malformation	11	5.9	6	4.6	17	5.4
Down syndrome	6	3.2	4	3.1	10	3.2
Genitourinary system defects	4	2.1	5	3.8	9	2.8
Head, face and neck defects	2	1.1	3	2.3	5	1.6

Types of neural tube defects: As indicated in Table 3, among the neural tube defects, spina bifida with or without menigocele/menigomyelocele was the most common (51.5%), followed by hydrocephaly (34.9%), anencephaly (6.8%), spina bifida with hydrocephaly (3.9%) and others (2.9%).

Factors associated with birth defects: As indicated in Table 4 and Table 5, absence of maternal folic acid supplementation, maternal history of chronic disease, history of medication and history of alcohol consumption during pregnancy were significantly associated with BDs.

Table 3: **The frequency of neural tube defects (NTDs) from 2015-2017 in FHRH and DMRH, 2018**

Variables	Frequency (n=103)	%
Spina bifida (lumbar, sacral, thoracic and cervical)	53	51.5
Hydrocephaly	36	34.9
Anencephaly	7	6.8
Spina bifida with hydrocephaly	4	3.9
Others*	3	2.9

*Spina bifida with cardiovascular system defects and anencephaly with limb defects.

Table 4: **The associated factors of birth defects in study subjects in FHEH and DMRH, 2018**

Variables		Frequency (n=321)	%
Maternal folic acid supplement	Yes	188	58.6
	No	133	41.4
Maternal history of alcohol intake	Yes	167	52.0
	No	154	48.0
Maternal history of chronic disease	Yes	142	44.2
	No	179	55.8
Types of chronic disease*	DM	53	37.3
	HIV/AIDS	44	31.0
	HTN	28	19.7
	Epilepsy	13	9.2
	CKD	4	2.8
Maternal history of medication	Yes	158	49.2
	No	163	50.8
Types of drug	Antiretroviral	35	22.2
	Insulin	32	20.3
	Antiepileptic	8	5.1
	Antihypertensive	21	13.3
	Drug name not recorded	62	39.2
Family history of BD	Yes	153	47.7
	No	168	52.3

*DM (diabetes miletus), HIV/AIDS (human immunodeficiency virus/acquired immune deficiency syndrome), HTN (hypertension), CKD (chronic kidney disease)

Infants born from mothers who did not have folic acid supplementation during pregnancy were 6.54 times [AOR = 6.54, 95% CI: 3.54-12.08)] more likely to have BDs compared to those who had folic acid supplementation. Infants of mothers who had a chronic disease during pregnancy, who took drugs or who had consumed alcohol during pregnancy were 4.05 times [AOR = 4.05, 95% CI: 2.27-7.21)], 3.55 times [AOR = 3.55, 95% CI: 1.98-6.38)] and 2.02 times [AOR = 2.02, 95% C: 1.13-3.60)], respectively, more likely to have BDs (Table 5).

Table 5: **Multivariate analysis of risk factors for birth defects (BDs) in study subjects in FHRH and DMRH, 2018**

Variables		Birth defect		COR* (95% CI)	AOR** (95% CI)	p-value
		Yes	No			
Sex of infants	Male	60	129	0.93 (0.58-1.49)	0.68 (0.38-1.21)	0.190
	Female	44	88	1	1	
Family residence	Urban	47	97	1.02 (0.64-1.63)	1.66 (0.90-3.04)	0.103
	Rural	57	120	1	1	
Maternal folic acid supplementation during this pregnancy	Yes	33	155	1	1	
	No	71	62	5.38 (3.23-8.93)	6.54 (3.54-12.08)	0.000
Maternal history of alcohol during this pregnancy	Yes	62	105	1.58 (0.981-2.53)	2.02 (1.13-3.60)	0.018
	No	42	112	1	1	
Maternal history of chronic disease	Yes	72	70	4.72 (2.85-7.82)	4.05 (2.27-7.21)	0.000
	No	32	147	1	1	
Maternal history medication during pregnancy	Yes	73	31	3.66 (2.22-6.03)	3.55 (1.98-6.38)	0.000
	No	31	132	1	1	

*COR = crude odds ratio; **AOR = adjusted odds ratio (adjusted for socio-demographic and other associated factors)

Discussion

The present study has observed a high prevalence of BDs among newly born infants and identified the associated risk factors. The most frequent types of BD were neural tube defects, followed by oro-facial clefts, cardiovascular system defects and upper and lower limb defects. A lack of folic acid supplementation, presence of chronic disease, intake of drugs and alcohol consumption during pregnancy were significantly associated with birth defects.

The current research findings are in line with a study of newborn infants conducted in the city of São Paulo, Brazil, which showed a BD prevalence of 1.6% (10). However, the prevalence of BDs observed in the present study was slightly less than that reported in another prevalence study conducted in Ethiopia

(1.96%) (9). This discrepancy might be due to the fact that this study included two national referral hospitals, including the Black Lion Hospital, where cases from different parts of the country are referred to for treatment and better management. A lower prevalence of BDs (12.5 per 1,000 live births) has been reported by a study carried out in India, where the data were collected from a single hospital (11). A much higher prevalence of BDs (4.1%) has been reported in a study conducted in Pakistan (12). This could be explained by the fact that the study was conducted in a hospital setting where only those infants who needed special care were admitted.

The current study shows that BDs were more frequent in males (59%) than in females (41%), which is in agreement with the finding of another study conducted in Ethiopia (58.5%) (9).

The most common form of BD was NTD, followed by OFC, while the least frequent were genitourinary system defects and head, face and neck defects, respectively. Similar frequencies of types of BD have been reported in studies conducted in Tanzania and Nigeria (13, 14). However, in a previous study conducted in Ethiopia (9), OFC was the most frequent type of BD, albeit by a slight margin. This may be expected, given that the study included the Black Lion Hospital, where as noted above, BD cases, including OFC, from different parts of the country are referred to for treatment and better management. On the other hand, infants born with NTDs are usually still births. Other investigations have reported that upper and lower limb defects (15) and congenital heart defects (16, 17), respectively, are the most prevalent BDs. These inconsistencies may be due to different maternal exposures to teratogens.

The present study shows that there is strong relationship between the prevalence of BDs and the lack of maternal folic acid supplementation during pregnancy, the presence of chronic disease, the intake of drugs, and the consumption of alcohol during pregnancy. Infants born from mothers who did not get folic acid supplementation during pregnancy were 6.54 times more likely to have BDs compared to infants born from mothers who took folic acid supplementation. This finding is in agreement with a study which reports that folic acid opponent drugs increase the possibility of BD, and that folic acid supplementation lowers the risk of BDs (18). Our finding is also in accordance with a study conducted in Texas, which reports that maternal folic acid supplementation significantly decreases the prevalence of NTDs (19). Maternal folic acid supplementation, especially one month before pregnancy and throughout the first trimester, significantly decreases BDs, mainly NTDs (20-23). In Ethiopia, the magnitude of NTDs is relatively high, which may be attributed to the low coverage of maternal folic acid usage (1.92%) (24). Even though, in Ethiopia, the policy for folic acid allocation is well established by the Federal Ministry of Health, pregnant mothers' folic acid usage is still low. This might be due to the lack of knowledge of health care providers, the community and pregnant mothers in terms of the importance of maternal folic acid supplementation during pregnancy (24).

Infants born from mothers who had a chronic disease during pregnancy were 4.05 times more likely to have BDs compared to infants born from mothers who did not have chronic diseases. The presence of chronic disease during pregnancy as a risk factor for BD is documented in text books (1). The finding of our investigation was also supported by studies conducted in Pakistan (25) and in the USA (26). Another study conducted in Canada also reported that several chronic maternal diseases, including diabetes, hypertension, connective tissue disorders and congenital heart disease confer an increased risk of BDs in offspring (27). Unlike our findings, however, research conducted in California reports that the magnitude of infants born with BDs from mothers who had chronic diseases was relatively low (28). A lack of clear knowledge about exactly when in the embryonic periods pregnant mothers develop chronic disease may be a factor in this discrepancy.

Another factor that had a significant association with BDs in the current study was maternal intake of drugs during pregnancy. Infants born from mothers who took drugs during pregnancy were 3.55 times more likely to have a BD compared to infants born from mothers who did not take any types of drug during pregnancy. This finding is congruent with the findings of other studies which report that maternal exposure to nitrate from drinking water and diet are risk factors for BDs (1, 29). The consumption of both prescribed and self-administered drugs during pregnancy have adverse effects on the development of the fetus (30).

Moreover, infants born from mothers who consumed alcohol during pregnancy were found to be 2.02 times more likely to have BDs compared to infants born from mothers who did not. Pregnant mothers drinking any amount of alcohol during early pregnancy had direct effects on the growth and morphogenesis of fetuses (31-33). In a study of rats, the use of an ethanol liquid diet for one month prior to conception and during development distorted the usual blueprint of myelination in rat progeny. It is highly likely that myelin developmental disorders cause other BDs (32).

Conclusions:

The present study has observed a comparatively high prevalence of BDs among newborn infants. Male infants were more likely to have BDs compared to females. The most frequent types of BD were NTDs followed by OFCs. Among NTDs cases identified, spina bifida was the most frequent. Absence of maternal folic acid supplementation during pregnancy, presence of chronic diseases, intake of drugs and consumption of alcohol during pregnancy were significant risk factors for the development of BDs.

The findings of the current investigation have shown that the prevalence of BDs in the East and West Gojjam zones of Northwest Ethiopia is unacceptably

high. Therefore, educating women of reproductive age and the community at large on BDs and the associated risk factors is critical, as lack of awareness is a major problem in the area.

The present study has given an insight into the magnitude of the problem of BDs and provided baseline data for future detailed studies, as there was very little data available previously. In addition, information from this study would be useful in developing strategies for the prevention of birth defects as well as for improved management and rehabilitation of surviving victims of BDs. Further detailed, nationwide, multicenter, retrospective/prospective investigations should be conducted to influence decision-making.

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