Original article:

Risk Factors and Complications of Newborns with Birth Defect: A Hospital based Case-Control Study

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Abstract:

Background: Birth defect is one of the most important causes of neonatal mortality worldwide. In a developing country like Bangladesh many possible factors for birth defects are present which should be identified. This study was performed to determine those risk factors of birth defect and complications associated with it. ***Materials and Methods:*** A hospital based matched case-control study was conducted from August 2015 to July 2016 in department of Neonatology along with Obstetrics and Gynecology at BSMMU. A total of 98 mother-infant pair (49 babies with birth defect as cases and 49 healthy babies without any birth defects as controls) was included in the study. For each case, a gestational age, sex and post-natal age matched control was taken. Data was collected by face to face interview. Univariate and multivariate conditional logistic regression models were computed to examine the effect of independent variables on outcome variable using SPSS 23.0. Variables with p-value <0.05 were considered statistically significant. ***Results:*** The mean (± SD) birth weight for cases and controls were 2718.37 (±756.9) grams, and 2617.14 (±978.8) grams respectively. Cardiovascular system was the predominant system (21%) involved in birth defects. Maternal age between 20-29 years (AOR: 4.69; 95% CI 1.078, 20.448), less than four antenatal care visits (AOR: 10.07; 95% CI 2.816, 36.0), no multivitamin intake (AOR: 7.38; 95% CI 1.791, 30.365) and presence of maternal diabetes (AOR: 0.194; 95% CI 0.047, 0.799) were significantly associated with birth defects among newborns. Sepsis, asphyxia, hypoglycemia and dyselectrolytemia were the most prevalent problems among these babies. The need of intravenous fluid, thermal care, antibiotics and mechanical ventilation was also high among the cases. ***Conclusion:*** Birth defect is an upcoming issue in current newborn health situation which need to be prioritized. Significant risk factors should be addressed timely for early diagnosis and proper management of these babies can help in reduction of mortality.

Keywords: *Birth defects, Frequency, Risk factors, Congenital anomalies*

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Introduction

Birth defects are structural or functional anomalies, including metabolic disorders, which are present at the time of birth[1]. With significant improvement of child health care overall childhood mortality has been decreased but the impact of birth defect is increasing day by day specially in developing countries. Birth defect is an important cause of neonatal and infant morbidity and mortality[2]. Every year more than 8.14 million children are born with a serious birth defect, due to genetic or environmental causes. Prevalence of birth defect in the South East Asia region ranges

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between 54.1 and 64.3 per 1000 live births and in Bangladesh 58.6 /1000 live births that contributes to about 5–7% of mortality[3].

Many studies have been conducted to determine the association of various risk factors with the incidence of birth defects. About 60% of the causes of congenital anomalies in humans are still unknown. However, in about 25% of congenital anomalies, the causes seem to be "multifactorial", indicating a complex interaction between genetic and environmental risk factors[1]. Several risk factors have been found to be associated with birth defect such as parental consanguinity, advanced maternal age, low birth weight, folic acid deficiency, anaemia, cigarette smoking, certain environmental, chemicals and high doses of radiation[4-5].

The pattern of congenital anomalies varies from region to region and also over time [6]. Congenital anomalies that involve the CNS, cardiovascular and musculoskeletal systems have been reported to be the most common[2,7]. Serious birth defects can be lethal. For those who survive, these disorders can cause lifelong mental, physical, auditory or visual disability[3, 8]. These defects therefore require early identification and immediate management.

In a developing country like Bangladesh birth defect is one of the four major leading causes (prematurity, asphyxia, neonatal sepsis, birth defects) of neonatal mortality and it constitutes about 12% of all neonatal deaths[9]. But there are only few hospital based studies in this topic. In a previous research conducted in Bangladesh, the prevalence rate of birth defect was found 3.68% and neural tube defects were highest, 33.33% among those defects[10]. Documentation regarding birth defect is necessary to know the magnitude, associated risk factors and immediate outcome for proper management of anomalous babies and to develop health programs for prevention of this condition. So, this study aimed to determine the common risk factors of birth defect and to identify the complications among those newborns in a tertiary care hospital in Dhaka, Bangladesh.

Materials and Methods

A hospital based matched case-control study was conducted from August 2015 to July 2016 in department of Neonatology and department of Obstetrics and Gynecology in Bangabandhu Sheikh Mujib Medical University (BSMMU), with the approval of Research Ethics Committee. Sample size was calculated by using formula of two proportions. All neonates born with birth defects in this center were included as cases. For each case, a gestational age, sex and post-natal age matched newborn with no birth defect was taken as control born immediately after birth of an anomalous baby. After delivery, routine care was given to all babies with or without birth defect. Soon after reporting, birth defect cases were examined meticulously by the investigator. Birth defects were classified according to ICD-10 (International Classification of Disease -10) [11]. A face to face interview was taken with mother or other caregiver and medical records were reviewed to identify risk factors.

In total, 22 variables were analyzed: fifteen maternal, four neonatal and three related to the conditions of the delivery. The maternal variables analyzed were: maternal age, education, occupation, parity, number of antenatal visits, presence of consanguinity, H/O periconceptional folic acid & multivitamin intake, presence of diabetes, hypertension and infection, drug history, smoking habit, passive smoking, alcohol intake, any radiation exposure and whether belonged to low socioeconomic condition etc. The variables related to labor condition were: type of pregnancy, mode of delivery and gestational age. The studied neonatal variables were gender, birth weight, fetal growth rate and APGAR score at 1st and 5th minutes respectively. Necessary radiological, hematological, biochemical and when possible, genetic investigations were done to confirm birth defect. Complications, management options and outcome (discharge/ referred /death) were documented. Neonates who left hospital against medical advice were excluded from the study. After collection, data was analyzed using the statistical package for social sciences (SPSS) version

23.0. Quantitative data were expressed as mean ± standard deviation and categorical data were presented as frequency. Chi square test was performed to compare qualitative variables and Independent sample t test was performed to compare quantitative variables. Association of risk factors was assessed with univariate and multivariate conditional logistic regression tests to see the odd ratio. P-values <0.05 were considered statistically significant.

Ethical clearance: The study was approved by ethics committee of BSMMU. Ethics Committee approval number and date: BSMMU/2015/11605

Results

Forty-nine cases and their matched forty-nine controls were enrolled in the study. The combination of two or more defects was observed in 31% of all cases. From figure 1 we can see that cardiovascular system (21%) was predominantly involved. Baseline characteristics like mean birth weight (cases: 2718.37 ±756.952 and controls: 2617.14 ± 978.849 g) were similar in both groups. Univariate analysis of maternal, delivery and neonatal factors were done (Table 1-2, figure 2). In Table 3, multivariate analysis of significant maternal variables showed that maternal age between 20-29 years was 3.7 times more in case of birth defect group. Less than four antenatal care visits and absence of multivitamin intake were also found significantly associated with birth defect. Similarly, presence of maternal diabetes was found as an independent risk factor for birth defect (OR =4.472, 95% CI= 1.086-18.409, p=0.038). Twenty six percent babies with birth defect needed Bag mask ventilation. About two third of cases required admission in neonatal intensive care unit (p value=0.027). Newborns with birth defect had several co-morbidities like sepsis, asphyxia, hypoglycemia, dyselectrolytemia which were significantly higher (p value <0.05) than their matched controls (Table 4). During management of these babies, requirement of intravenous fluid (p<0.001), thermal care (p=0.040), antibiotics (p=0.001) and mechanical ventilation (p=0.007) was also higher (Figure 3). Newborns having birth defect had higher mortality (p value=0.0001) than those without birth defect.

Discussion

The pattern of birth defect may vary over time or with geographical location, reflecting a complex interaction of known and unknown genetic and environmental factors including socio-cultural, racial and ethnic variables[12]. With improved control of infections and nutritional deficiency diseases, birth defects have become important causes of perinatal mortality in developing countries like Bangladesh.

The result of the present study demonstrated that mean gestational age of the birth defect group was 35.96 ± 2.55 weeks. This finding is consistent with the study done by Fatema K et al (2011) where they have found babies having birth defect with gestational age of 34-36 weeks (46.67%)[10]. This is because antenatal visit in most of the mothers were less <4. They first came in contact with the health personnel or health facilities in late third trimester. It is noteworthy that all the subjects made at least one or two antenatal visits to the health personnel for antenatal checkup. Regular antenatal checkup may help early diagnosis and termination of fetuses incompatible with life.

In our study, birth defect involving most common body system was cardiovascular system (21%) followed by central nervous system (19%) and musculoskeletal system (19%); patterns are similar with other studies [2, 13-14]. This increase in defect of cardiovascular system might be due to availability of bedside Echocardiogram by which many CVS defects were diagnosed early, those remained undetected previously.

Present study revealed that birth defect cases were significantly more frequent among mothers age between 20-29 years (p value= 0.022). It might be due to number of mothers with age range 20-29 years were high in both groups. Similar findings were found in other studies conducted in Bangladesh and India [10, 12]. Current study also showed that diabetes mellitus was the only maternal disease having significant association with birth defect (p value=0.038, OR= 4.472, 95% CI = 1.086-18.409) which is comparable to other studies[10, 15]. Many other

maternal diseases may occasionally lead to increased risk of birth defects such as hypertension and hypothyroidism, but findings were not statistically significant in this study. As the study center was a tertiary care hospital, all complicated cases were used to come here from peripheral hospitals. That's why other maternal illnesses were found nearly similar in both groups.

In this study no data on maternal smoking and alcohol intake was found. This may be due to the fact that cigarette smoking and alcohol intake are not common in Bangladeshi women. In addition, under ascertainment bias could have also affected the result of the present study due to non-reporting of family history because of shame. Single delivery was predominant (96%) in our study which is consistent with the study finding of Fatema K et al (2011) done in BSMMU [10]. More male babies with birth defect were noted in this current study (M: F =2:1) which is comparable to study done by Sarkar S et al (2013)[12]. It may be because of the fact that the females were afflicted with more lethal congenital malformations and could not survive to be born with signs of life.

In this study 5 minutes APGAR score was found low in babies with birth defect (p value=0.001) and this finding is similar with other study results[16]. This is due to major malformations leads to intrauterine hypoxic state which ultimately turns into perinatal asphyxia. Present study aimed to detect complications of babies with birth defect in terms of their associated morbidities. But there is scarcity of studies in this aspect. Findings of this study suggest that sepsis, asphyxia, hypoglycemia, dyselectrolytemia were significantly higher (p value <0.05) in these babies. Need of intravenous fluid (p=0.0001), thermal care (p=0.040), antibiotics (p=0.001) and mechanical ventilation (p=0.007) was also higher. Newborns having birth defect had higher (31%) mortality, (p value=0.0001) than those without birth defect. There are few studies those estimate mortality rate due to birth defect[14-16].

Conclusion

Our present study has identified several risk factors for birth defects among newborn. We have found that maternal age from 20 to 29 years, less frequent (< 4) antenatal visits and not taking any multivitamin during pregnancy is significantly associated with birth defects among newborns. We have also seen that mothers with no diabetes works as protective factor than those having mothers with diabetes. Health professionals should be vigilant in early detection and management of complications during pregnancy. Additionally, efforts should be done to improve living standard and lifestyles of mothers. Community based studies are needed to better address household and environmental factors with observation.

Conflict of Interest: None

Authors's contribution:

Data gathering and idea owner of this study: Dr. Mohammod Shahidullah, Dr. M A Mannan, Dr. Sharmin Afroze

Study design: Dr. M A Mannan, Dr. Sanjoy Kumer Dey , Dr. Sharmin Afroze

Data gathering: Dr. Sharmin Afroze, Dr. Ismat Jahan

Writing and submitting manuscript: Dr. Sharmin Afroze, Dr. Sadeka Choudhury Moni, Dr. Kamrul Hassan Shabuj

Editing and approval of final draft: All authors participated in editing and approval of final draft

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Table 1: Distribution of maternal and delivery variables among cases and controls

Variable	Case (Newborns with Birth Defect) N= 49 (%)	Control (Newborns without Birth Defect) N= 49 (%)	p value*
Maternal variables:			
Age			
<20 years	2 (4)	5 (10.2)	0.239
20-29 years	36 (73)	25 (51)	**0.022**
30-39 years	9 (18.3)	13 (27)	0.333
≥ 40 years	2 (4)	6 (12)	0.140
Education			
High school or below	19 (39)	15 (31)	0.396
Higher 2ndary school	19 (39)	20 (41)	0.836
Degree or equivalent	11 (22.4)	14 (29)	0.665
Occupation			
Housewife	37 (76)	41 (84)	0.316
Works outside house	12 (24.4)	8 (16.3)	
Parity			
Primipara	26 (53)	15 (31)	**0.024**
Multipara	23 (47)	34 (69)	
Number of Antenatal visits			
< 4 visits	22 (45)	5 (10)	**0.000**
≥ 4 visits	27 (55)	44 (90)	
Consanguinity	9 (18)	6 (12)	0.400
H/O Peri-conceptional Folic acid intake	4 (8)	3 (6)	0.695
H/O Multivitamin intake	31 (63)	44 (89)	**0.002**
Maternal Illness During Pregnancy	28 (57)	24 (49)	0.418
H/O drug intake	23 (47)	21 (43)	0.685
Passive smoking	15 (31)	21 (43)	0.209
Low socio-economic condition	21 (43)	20 (41)	0.838
Delivery variables:			
Type of pregnancy			
Single pregnancy	47 (96)	48 (98)	0.988
Multiple pregnancy	2 (4)	1 (2)	
Mode of delivery			
Caesarian	40 (82)	44 (90)	0.248
Vaginal	9 (18.3)	5 (10.2)	
Mean Gestational age (wks)	35.96 ± 2.55	36.02 ± 2.34	0.815

*Statistical test: Chi square test and Independent Sample t test (*p value considered significant when <0.05)*

Table 2: Distribution of Neonatal variables with birth defects (cases) and their matched controls

Variables	Case (Newborns with Birth Defect) N= 49 (%)	Control (Newborns without Birth Defect) N= 49 (%)	p value*
Sex			
Male	33 (67)	33 (67)	0.988
Female	15 (31)	16 (33)	
Ambiguous	1 (2)	-	
Birth weight			
1000- <1500 g	3 (6)	9 (18)	0.064
1500- <2500 g	16 (33)	17 (35)	0.988
2500- < 4000 g	26 (53)	16 (33)	**0.039**
≥ 4000 g	3 (6)	7 (14.2)	0.182
Mean Birth weight (g)	2718.37±756.952	2617.14 ± 978.849	0.071
Fetal growth at Gestational age			
SGA	4 (8)	5 (10.2)	0.727
AGA	35 (71.4)	39 (80)	0.475
LGA	5(10.2)	4 (8)	0.727
IUGR	5 (10.2)	2 (4)	0.239
APGAR at 1st minute			
≥ 7	34 (69)	41 (84)	**0.036**
4-6	11 (22)	8 (16)	
0-3	4 (8)	-	
APGAR at 5th minute			
≥ 7	35 (71)	47 (96)	**0.001**
4-6	11 (22)	2 (4)	
0-3	3 (6)	-	

*Statistical test: Chi square test and Independent Sample t test (*p value considered significant when <0.05)*

Table 3: Conditional Binary Logistic regression analysis of risk factors for Birth Defect (Maternal Variables)

Risk Factor	β*	OR*	95% CI*	p value*
Age (20-29 years)	1.546	4.69	1.078-20.448	0.039
Parity (Primipara)	0.638	1.89	0.649-5.519	0.243
Antenatal visits (<4 times)	2.309	10.07	2.816-36.00	<0.001
Multivitamin intake (No)	1.998	7.38	1.791-30.365	0.006
Presence of Maternal Diabetes	-1.642	0.194	0.047-0.799	0.023

**β= Beta co-efficient, OR= Odds Ratio, CI= Confidence interval, p value significant when <0.05*

Table 4: Comparison of Co-morbidities associated in Newborns with and without Birth Defects

Variables	Case (Newborns with Birth Defect) N= 49 (%)	Control (Newborns without Birth Defect) N= 49 (%)	p value*
Prematurity	25 (51)	25 (51)	1.000
Sepsis	31 (63)	21 (43)	**0.043**
Asphyxia	13 (27)	5 (10.2)	**0.037**
Jaundice	16 (33)	17 (35)	0.831
Respiratory Distress	22 (45)	17 (35)	0.302
Meningitis	3 (6)	-	0.079
Hypothermia	3 (6)	2 (4)	0.646
Hypoglycemia	4 (8)	-	**0.031**
Apnea	1 (2)	1 (2)	1.000
Dyselectrolytemia	10 (20)	-	**0.001**

*Statistical test: Chi square test (*p value considered significant when <0.05)*

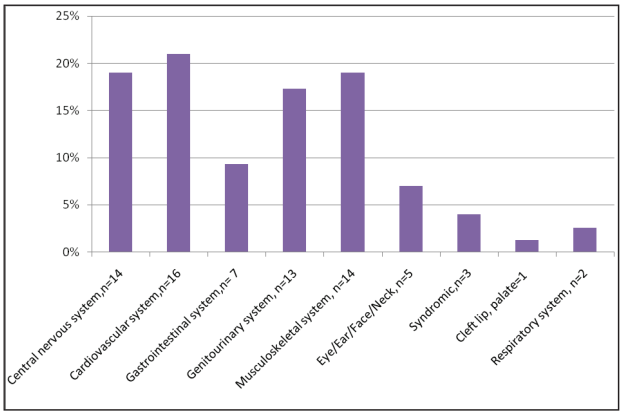
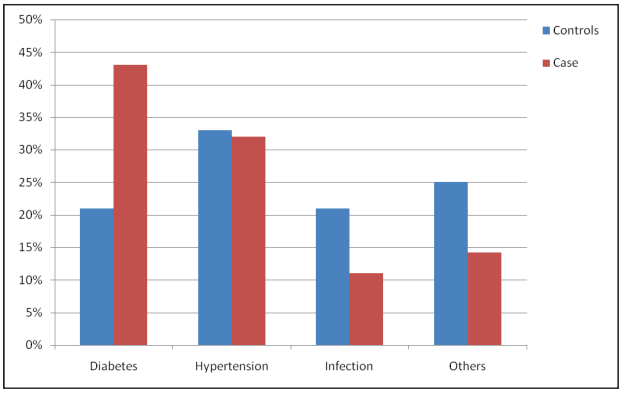
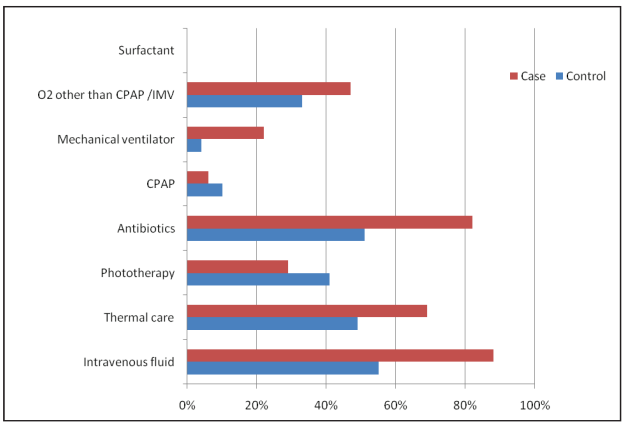


Figure 1: Distribution of Birth Defect according to ICD-10 (n=75; multiple birth defects of one child)



*Statistical test: Chi square test (*p value considered significant when <0.05)*
P value for presence of maternal diabetes = 0.029(more among cases than controls)
Figure 2: Distribution of Maternal Illnesses among Newborns with and without Birth Defect



*Statistical test: Chi square test (*p value considered significant when <0.05) p value for intravenous fluid =0.000, thermal care=0.040, antibiotics=0.001and mechanical ventilator=0.007)*
(O2= oxygen, CPAP= Continuous Positive Airway Pressure, IMV= Intermittent Mandatory Ventilation)
Figure 3: Distribution of management required in Newborn with and without Birth Defect

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