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Original Article

Risk Factors of Birth Defects: A Case-control Study in a Tertiary Level Hospital

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Abstract:

Worldwide birth defects are one of the main causes of morbidity and disability among children. The risk factors vary significantly by geography, depending on local environmental and genetic factors. Our aim was to ascertain the local risk factors for birth defects, which is the first step toward devising preventive policies. From February 2018 to October 2019, this case-control study was undertaken at Sir Salimullah Medical College and Mitford Hospital, Dhaka, in the Department of Neonatology and Obstetrics. During this period 49 admitted newborns with birth abnormalities were selected as cases, and children of similar gestational age, sex, and post-natal age were selected as controls for each case. To determine the risk factors for birth abnormalities, in-depth interviews with mothers regarding their demographic and obstetric histories were recorded and analyzed. We found that mothers aged 26-30 years had a significantly increased risk of birth defects ($p = 0.01$). Additionally, mothers who had a history of diabetes had a considerably higher risk of delivering a child with birth defects ($p = 0.03$). During the pregnancy period, mothers who attended <4 antenatal care (ANC) visits and mothers who did not take iron or folic acid supplementation had a higher risk of birth defects ($p = 0.02$ and $p < 0.01$, respectively).We found out that the majority of birth defect risk factors are preventable or controllable. By promoting appropriate antenatal care and educating mothers about relevant regional risk factors, the occurrence of birth defects can be lowered significantly.

Keywords: Birth defects, Newborn, Risk factors

Introduction:

Birth defects are a major contributor to neonatal mortality and morbidity worldwide[1]. According to World Health Organization (WHO), birth defects are structural or functional abnormalities, including metabolic disorders, which are present from birth[2]. Globally, an estimated 2-6% of all births are affected by birth defects[3-8]. But the rate of birth defects vary substantially from region to region, ranging from 39.7 per 1000 live births in France to up to 82.0 per 1000 live births in Sudan[3, 9]. Furthermore, 95% of children who die as a result of birth defects are from middle- and low-income countries[3,4,10]. Birth defects occur at a rate of 58.6 per 1000 live births in Bangladesh, accounting for nearly 12% of neonatal deaths[3,11-14].Providing treatment and rehabilitation for the surviving children also involves a significant emotional and financial drain on the individual, family, society, and state[9,10,14-18].

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Several studies have been conducted in an attempt to ascertain the causes of birth defects. However, between 40% and 60% of birth defects are found to be caused by unknown factors with polygenic or multifactorial etiologies[9,16,19]. Among the rest, genetic factors, single gene mutations, chromosomal abnormalities, and various maternal illnesses have been suggested[4,9,17]. Meanwhile, a variety of risk factors for birth defects have been identified, including parental consanguinity, advanced maternal age, diabetes, infection, iron and folic acid deficiency, substance abuse, various medications, radiation, hyperthermia, chemical exposure, and uterine anomalies[11,17,19-23].

Data from high-income countries show that up to 70% of birth defects can be prevented and the affected children can be provided with life-saving or disability-reducing cares[3]. However, the pattern of birth defects and the support for the affected children vary by region due to environmental factors, individual habits, and cultures[11]. To know the magnitude of birth defects and devise preventive measures, it is critical to understand the local risk factors[4,6, 8,11,15,16,24].

Bangladesh is a densely populated country, with a World Bank-estimated midyear population growth rate of 17.5 live births per 1000 in 2020[25]. Unplanned pregnancy, consanguineous marriage, improper or non-existent antenatal care, and maternal malnutrition are only a few of the prevalent issues faced by pregnant women in Bangladesh[26]. Additionally, there has been a rise in exposure to teratogens, including pesticides and drugs[9]. However, only a few studies exist in Bangladesh on the risk factors for birth defects.

The purpose of this study was to identify the risk factors for birth defects among neonates at a tertiary care hospital in Bangladesh in order to contribute to the development of local data for future preventive measures.

Materials and Methods:

This hospital based matched case-control study was conducted in the neonatal intensive care unit (NICU) of the Department of Neonatology and the Department of Obstetrics and Gynecology, Sir Salimullah Medical College and Mitford Hospital (SSMCMH), Dhaka, from February 2018 to October 2019.

During this period, all children born at the department of Obstetrics or got admitted to the NICU of the Department of Neonatology with at least one birth defect were included as cases. Children with matched gestational age, sex, and post-natal age who did not have a birth defect were selected as controls for each case. The investigators assessed for birth defects following delivery or admission of the newborns. Care to the cases and controls were provided as per standard management guidelines. Neonatal characteristics were collected, and mothers were interviewed face to face using a pre-structured questionnaire. In addition, the medical records of the mothers were also reviewed.

To classify birth defects, the International Classification of Disease-10 (ICD-10) was used. Maternal demographics, co-morbidities, obstetric history, drug history and antenatal care history were asked in detail to determine risk factors for birth abnormalities.

A total of 49 neonates with birth defects were selected as cases and 49 as control. The parent or guardian of each participant signed written informed consent forms. The Institutional Review Board (IRB) and Ethics Committee of SSMCMH granted ethical approval for the study.

SPSS version 23.0 (IBM Corp. Released 2012.IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) was used to analyze the data. Mean ± standard deviation and frequency were used to present the quantitative and categorical data, respectively. Chi-squared test was used to compare qualitative variables, t-test was used to compare quantitative variables. Univariate and multivariate logistic regressions were used to analyze the odd ratio of risk factors. Statistical significance was defined as a P-value <0.05.

Results:

During this period, 49 newborns with birth defects were selected as cases, and for control, 49 newborns having the same age, gender, and post-natal age but without birth defects were included.

Table I shows the maternal demographic and obstetric characteristics of the case and control groups. The majority (57.1%) of the mothers of the cases were between the age of 26-30 years, whereas for the control group, the majority (44.9%) belonged to the 21-25 years age group and it was statistically significant ($p <0.01$). Most of the mothers, both from case and control groups, were from the low and middle socioeconomic classes. Based on the personal history and co-morbidities, mothers of the case group had statistically significant higher numbers of passive smoking and diabetes.

Table I: Distribution of maternal demographic and clinical characteristics of the mothers from case and control groups

Characteristics	Case N = 49 n, (%)	Control N = 49 n, (%)	p value*
Age			
<20	5 (10.2)	8 (16.3)	<0.01
21-25	11 (22.4)	22 (44.9)	
26-30	28 (57.1)	16 (32.7)	
31-35	5 (10.2)	3 (6.1)	
Socioeconomic status			
Low	29 (59.2)	25 (51.0)	0.24
Middle	20 (40.8)	22 (44.9)	
High	0	2 (4.0)	
Personal history and co-morbidities			
Consanguineous marriage	7 (14.3)	2 (4.0)	0.16
Smoking (Passive)	15 (30.6)	6 (12.2)	0.04
Bronchial asthma	4 (8.2)	2 (4.0)	0.67
Diabetes	11 (22.4)	3 (6.1)	0.04

*Two-tailed Fisher's Exact Test and Chi-square test were done to calculate the p values

The obstetric history of the mothers is illustrated in Table II. There were no significant differences between different parity. But only 1 mother (2%) from the case group took 4 antenatal care visits and the number of antenatal care visits was significantly less than the control group. Less than half of the mothers (46.9%) took iron and folic acid supplementation during pregnancy in the case group, which was significantly less than the control group (p = 0.01). Only 2 mothers of the case group had a history of offending drug consumption from pharmacy without the consultation of any physician, but we did not find any statistical significance. The mean gestational age for the case group was 36.02 ± 3.55 weeks and in the control group, it was 37.11 ± 2.04 weeks. We also did not find any statistical significance between vaginal and cesarean section delivery (p = 0.84) and plurality of the two groups was inclusive of any difference.

Regarding previous bad obstetric history, 4.1% had history of termination of pregnancy for malformation in the case group and none in the control group (p = 0.49). In the case group, 12.2% of the mothers had a history of spontaneous abortion, whereas none were in the control group and it was statistically significant (p = 0.02).

None of the mothers from the case or control groups had any history of radiation, alcohol consumption, fever with rash, previous stillbirths and history of birth defects in previous live births.

Table II: Obstetric characteristics of the mothers from case and control groups

Characteristics	Case N = 49 n, (%)	Control N = 49 n, (%)	p value*
Parity			
Primipara	28 (57.1)	20 (40.8)	0.16
Multipara	21 (42.9)	29 (59.2)	

Antenatal care visits (number)			
<4 visits	48 (98.0)	40 (81.6)	0.01
≥4 visits	1 (2.0)	9 (18.4)	
History of iron and folic acid intake	23 (46.9)	36 (73.5)	0.01
Any offending drug consumption	2 (4.0)	0	0.49
Mean gestational age (weeks)	36.02 ± 3.55	37.11 ± 2.04	0.06
Mode of delivery			
Vaginal	24 (49.0)	22 (44.9)	0.84
Caesarean section	25 (51.0)	27 (55.1)	
Plurality			
Single	48 (98.0)	47 (96.0)	1.00
Twin	1 (2.0)	2 (4.0)	
Previous bad obstetric history			
Termination of pregnancy for malformation	2 (4.1)	0	0.49
Spontaneous abortion	6 (12.2)	0	0.02

*Two-tailed Fisher's Exact Test and Chi-square test were do ne to calculate the p values

According to Table III, males were predominant in both case and control groups (61.2% and 53.1%, respectively) but it was not statistically significant (p = 0.54). However, statistical significance was observed between the birth weight of the children (p = 0.04).

Table III: Comparison of the child characteristics between the case and control groups.

Characteristics	Case N = 49 n, (%)	Control N = 49 n, (%)	p value*
Sex of the baby			
Male	30 (61.2)	26 (53.1)	0.54
Female	19 (38.8)	23 (46.9)	
Birth weight (gm)			
<1800	1 (2)	2 (4.1)	0.04
1800-2500	13 (26.5)	7 (14.3)	
≥2500	35 (71.4)	40 (81.6)	

*Two-tailed Fisher's Exact Test and Chi-square test were done to calculate the p values

During the conditional binary logistic regression analysis of the maternal risk factors, we have found statistically significant risk for birth defects among mothers between the age groups of 26-30 years, mothers who had a history of passive smoking, had <4 antenatal care visits, did not have history taking of iron and folic acid supplementation, history of diabetes and spontaneous abortion (Table IV).

Table IV: Binary logistic regression of the maternal variables for risk of birth defect

Risk factors	OR	95% CI	p value
Age (26-30)	2.75	1.20 to 6.26	0.01
Smoking (passive)	3.16	1.10 to 9.01	0.03
<4 Antenatal care visits	10.8	1.31 to 88.92	0.02
No history of iron and folic acid intake	0.31	0.13 to 0.74	<0.01
Spontaneous abortion	14.79	0.80 to 270.25	0.06
Diabetes	4.43	1.15 to 17.07	0.03

Discussion:

Each year, approximately 7.9 million children are born with birth defects worldwide, with the majority of these infants being born in middle- and low-income countries[3]. Birth defects vary by country due to a complex interaction of genetic, environmental, sociocultural, and ethnic factors[11]. Recognizing regional risk factors is the first step toward prevention.

Earlier research has suggested that maternal advanced age is related to an increased incidence of birth defects[7, 10]. However, we found that mothers aged 26-30 years were more likely than others to have children with birth defects. This finding is probably related to the fact that the majority of mothers in our sample were between the ages of 21 and 30, with very few mothers over the age of 30 years.

In our study, socioeconomic status made no statistically significant difference. However, research from middle- and low-income nations imply that mothers from impoverished families may be deficient in vital nutrients, which may result in a variety of birth defects. In this regard, it is worth noting that the majority of mothers in our study were from low- and middle-income families.

Although it is well established that consanguineous marriage increases the risk of birth defects[4,17,27,28], we did not observe any statistically significant difference. Mothers exposed to passive cigarette smoking had a significantly increased risk of delivering a child with a birth defect, which is consistent with earlier research[29, 30.] Additionally, we observed that maternal diabetes increased the likelihood of birth defects substantially. Similar outcomes have been observed from previous studies conducted in Bangladesh[11,16]. Other maternal conditions, such as hypothyroidism and hypertension, were not correlated to birth defects in our study, most likely due to a small number of cases. However, mothers who had a past history of spontaneous abortion had a higher incidence of birth defects in our study, which could indicate genetic defects.

In our study, no difference between different parities was found. However, Afroze et al. showed that the frequency of birth defects was considerably higher among primipara mothers[11]. On the other hand, Patra et al. reported that multiparity was associated with an increase in birth defects[28].

Mothers who did not receive prenatal care had a greater likelihood of birth defects than other mothers in our study. This is most likely because embryonic defects were discovered earlier in mothers undergoing routine ANC. Similarly, Afroze et al. and others reported that fewer antenatal care visits were associated with an increased chance of birth defect11.We identified that mothers who did not take iron or folic acid supplements during their pregnancy had a significantly higher risk of delivering children with birth defects. Similarly, Afroze et al., Harris et al., and others have reported similar findings[11,19].Although two of the mothers in the case groups had a history of self-medication without consulting a physician, we were unable to establish a statistically significant difference. However, past research indicates that taking non-prescribed drugs during pregnancy is associated with an increased risk of birth defects[4,10].

Previous research indicated that children born at a lower gestational age had a considerably increased risk of birth defects[17, 28]. This may be because children with birth defects were more likely to deliver prematurely. Similarly, we discovered a near-significant relationship between birth defects and lower gestational age ($p = 0.06$). Numerous studies have already established that males are predisposed to birth defects[8,10,28,31-34]. This could be because female fetuses are more prone to develop fatal abnormalities that preclude them from being born alive. Our study also found a male prevalence, although it was not statistically significant. Children with birth defects exhibited a considerably increased risk of low birth weight when compared to control groups. Previous studies have also shown that children with birth defects are more likely to have low birth weight1[6,17,28,32,33].

Our results demonstrate that risk factors and their prevalence vary according to region and that the majority of these risk factors are preventable. It emphasizes once again the importance of comprehending these critical factors in order to develop effective local preventative policies.

Limitation:

We used a small sample size to compare all the unusual risk factors that occur at a lower frequency, which may have resulted in inconclusive impacts. A large-scale multicenter study is necessary to more precisely determine the risk factors for birth defects.

Conclusion:

Our study identified several risk factors for birth defects, including maternal diabetes, prenatal exposure to smoking, inadequate antenatal visits, insufficient iron

and folic acid supplements, and a prior bad obstetric history. The majority of these factors are controllable or preventable. A significant reduction in the occurrence of birth defects is possible if policies aimed at increasing awareness of these preventable risk factors can be widely disseminated among mothers and healthcare providers.

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