

# Association of Congenital Heart Disease Among the Neonate-Children with Their Maternal Diabetes

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## ABSTRACT

The present study is a standalone piece of work in this area where the association of mother's Diabetes Mellitus (DM) and Congenital Heart Disease CHD of children were investigated. The present study was carried out in two hospitals in Dhaka city from June to December 2019. A total of 78 neonatal admitted children having heart disease were to the hospitals for treatment and was taken as study samples. The study applied logistic regression analysis and reported the odd ratio to identify the possible covariates that affect CHD. The present results represent that only 73% of the neonate had CHD problem, 85% of the neonate had cyanosis, 41% had resuscitation, 38% had chest inside, 33% showed murmur sound, 18% had GHTN and only 1% had Eclampsia. The present study identified that 63% of the neonate had Patent Arterial Duct (PDA) found in the ECHO results whereas Atrial Septal Defect (ASD) (67%) and Ventricular Septal Defect (VSD) (25%) were also found. Mothers were found with Diabetic Mellitus (50%), 87% of the neonates of diabetic mothers were experienced CHD than the 59% CHD of neonates of the non-diabetic mothers. Odds ratio from the log, it model shows that there is a 5.8 times higher risk of CHD in neonates if the mother has diabetes. Besides, mother's age possesses 1.14 times and unwanted event during pregnancy 4.2 times the risk of CHD among neonates. Also, the mother's higher weight can significantly reduce this probability of CHD. It may be concluded that, the incidence of Congenital Heart Disease (CHD) in Bangladesh is increasing. A significant association was found with mothers and family characteristics. Diabetic mothers and aged mothers have more tendencies to give birth to neonates with CHD problems. Unwanted events increase the risk of CHD of neonates. Change lifestyle of mothers and timely pregnancy may reduce the risk of neonate CHD.

## Introduction

Congenital Heart Disease (CHD) is the most common lesion among all types of neonatal disease in the world [1]. CHD is defined as a gross structural abnormality of the heart or intra-thoracic great vessels which potentially of functional significance [2]. Studies found that the incidence of CHD varies from 4/1000 to 50/1000 live birth and the relative frequency of different types of major form of CHD differs with variety of case context especially in stillbirth, spontaneous abortion and prematurity [3,4]. It is frequently reported that the CHD incidence is either constant or increasing worldwide [5,6]. There is no nationwide survey on congenital

heart disease of neonate children in Bangladesh, however, different studies suggest that the incidence of CHD in Bangladesh is around 18/1000, 15% in India, and 10% in Sri Lanka [6-8]. There are nine common lesions that constitute the 80% of the CHD where 36% Ventricular Septal Defect (VSD), 5% Atrial Septal Defect (ASD), 9% Patent Arterial Duct (PDA), 9% Pulmonary Stenosis, 5% Aortic Stenosis, 5% Coartation of Aorta, 4% Transposition of Great Arteries, 4% Tetralogy of Fallot etc. [5].

CHD is the most common lesion among all types of neonatal disease in the world. The exact causes of the congenital heart disease

are not clear, literature have identified that CHD are thought to be multifaceted and multi-factorial and results from a combination of genetic predilection and environmental stimulus and severity of the disease and needs different types of clinical interventions for their survival [9,10]. The most common neonatal congenital heart disease are cyanosis, heart failure, collapse, and abnormal clinical sign identified by regular examination for example, absent of femoral pulse or heart murmur sound [11]. The most common problems are cyanosis, clubbing, murmur, syncope, squatting, heart failure, arrhythmia, failure to thrive in the infant and children, and adolescent and the adults present with heart failure, murmur, arrhythmia, cyanosis hypertension, late consequences of previous cardiac surgery.

The incidence of CHD depends on many factors including biological factor, socio-economic factors, environmental factors, healthcare system, and even on the national economy. Besides, the CHD cases may also come from Down's syndrome babies, babies with diabetic mother, and babies with other congenital malfunctions. It is a matter of fact that most cases of CHD die in early infancy and some may manifest a delayed exposure. The prevalence rate of CHD in Bangladesh population is not known as there is no official representative survey in Bangladesh for that in the recent years. There are some small-scale studies that shown the prevalence rate of the CHD in that specific hospital, however, the research suffers from sample size biasness and endogeneity problem [12]. Several studies in Bangladesh reported that the prevalence rate of neonatal CHD is close to 6 to 25 per thousand live birth. Findings from the study based on the pediatric department of Rajshahi Medical College and Hospital showed that children from birth to until 12 years suffer from various CHD problems specially VSD (42.6%), TOF (18.3%), ASD (14.8%), PDA (7.8%) where murmur and cardiomegaly were the most important cardiac findings [13].

Similar studies were found that 65.38% were acyanotic and 34.42% cases were cyanotic, with the commonest CHD of VSD-33.33%, ASD-16.24%, TOF-11.54%, PDA -10.68% (Hoque et al., 2014); another study based on the Department of Paediatric Cardiology at National Institute of Cardiovascular Diseases, Dhaka, found that VSD-27.2% and TOF-20.5%. A study based on neonate children aged birth to 28 weeks gestational period were found that ASD-26%, VSD-16.9%, PDA-18%, TOF-14%, PS-7.75% with asymptomatic high-risk neonates contributing to early detection of many trivial lesions [14]. The causes of CHD are assumed to be associated with many other factors such as pregnancy factor, mother's diseases factors, father's disease factors, socio-economic characteristics, environmental characteristics and the healthcare system of the location. In a study conducted in 2000- 2001, found that diabetes mellitus of mother is associated with the infant's CHD. It was found that, pre-existing maternal diabetes is associated with a fivefold increase in the congenital heart disease [15]. Until 2009,

a study in Norway confirmed that this association of CHD and DM mothers is almost two to three fold than the non-DM mothers [16]. It is found that several researcher has identified the different type of CHD of neonate children in Bangladesh [17-19].

Justification of the study: In cases of adverse pregnancy outcome like complicated delivery, mother's and baby's illness or in any emergency psychological effects of the participants had been taken care of while asking question or collecting information. In this context, this study is the unique and standalone piece of research that studied the association of CHD of neonate children and mothers' diabetes after controlling for other socio-economics characteristics and other health related variables.

## Materials and Methods

A total of 78 children were selected who were admitted to the NICU for heart diseases. However, among them, not all children were detected CHD, rather other symptoms of respiratory problems. The mothers of the patients were interviewed based on their consent to take part in this study and their medical tests. The study examined their echocardiogram and other necessary examination, collected child and mother history of previous disease and mother's diabetic situation. Observational data was collected in the study and logistic regression analysis was conducted for identifying the association among the variables. The target populations are those who visited at Bangladesh Institute of Health Science (BIHS) and Universal medical College Hospital during their pregnancy. In Outpatient department, the study was carried out from July, 2019 to December 2019. Purposive sampling technique was adopted for selecting respondents. A structural questionnaire was used for correlation of necessary information. A check list or medical records were done for assessment of three trimester pregnant women condition. The Anthropometric data (height and weight) was collected based on standard methods. Chi square test was done between categorical variables to show the association between dependent and independent variables. Logistic regression was used for multi variants analysis to control the potential confounding factors.

## Results

### Socio-Economic Factors

The history of the mothers of the patients include mother's age, weight, doing exercise, number of pregnancies, unwanted pregnancy events, having hypertension, diabetes, health-seeking behavior, family history of hypertension, family income, neonatal congenital heart disease, types of heart disease, and different types of treatments (Table 1) . In the present study, it was found that 76% of the mother did exercise regularly during pregnancy. On average, there are 2.1 pregnancies for a mother in Bangladesh. About 35% of a mother faced unwanted events during the pregnancy such as abortion and other complications. 28% of the mothers had either high blood pressure or low blood pressure and they had to admit to

the hospital. However, 23% of the mothers in the collected sample, had hypertension. On average there were 3.2 doctor's checkups during the pregnancy (Table 1). Age and weight of mothers: In the present investigation, It was found that almost 70% of mothers were aged over 25 for their current pregnancies, 15% was found very young mothers who were aged 18 to 20 years and their average weight was 45.4 kg which was found to be lower weight according to WHO standard. The average weight of 26 to 30 years old mothers was 53 kg and the average weight of 31 to 42 years mother was 60.4 kg (Table 2).

**Table 1:** Summary statistics of the selected variables.

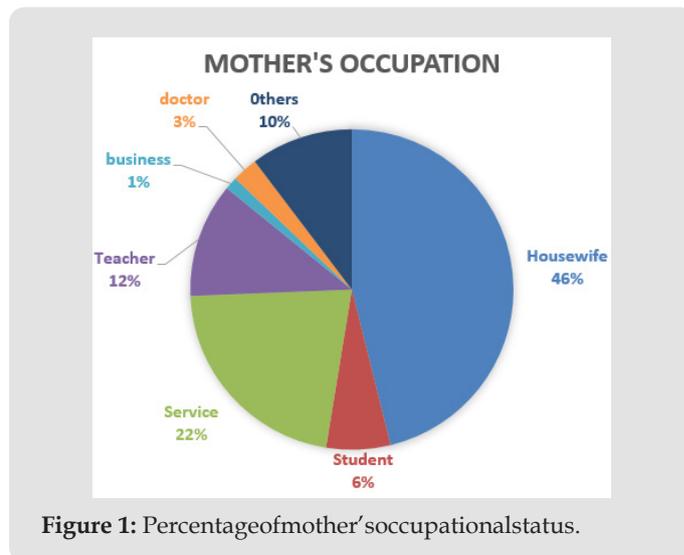
Variable	Total No.	Mean	Std. Dev.	Min	Max
Mother's age (years)	78	28.7	6.3	18	42
Family income (BDT)	78	48766	19142	2800	900000
Mother's weight (kg)	78	54.1	7.8	41	78
Birth trimester (week)	78	34.7	4.3	24	40
Mother exercises	78	76%	0.5	0	1
Number of Pregnancies	78	2.1	1.1	1	5
Unwanted events in last pregnancies	78	35%	0.5	0	1
Hospital admission due to blood pressure	78	28%	0.5	0	1
Hypertension	78	23%	0.4	0	1
Hypertension of mother in last pregnancy	78	24%	0.4	0	1
Number of checkups in current pregnancy	78	3.2	1.2	0	5

**Table 2:** Mother's age in the sample size.

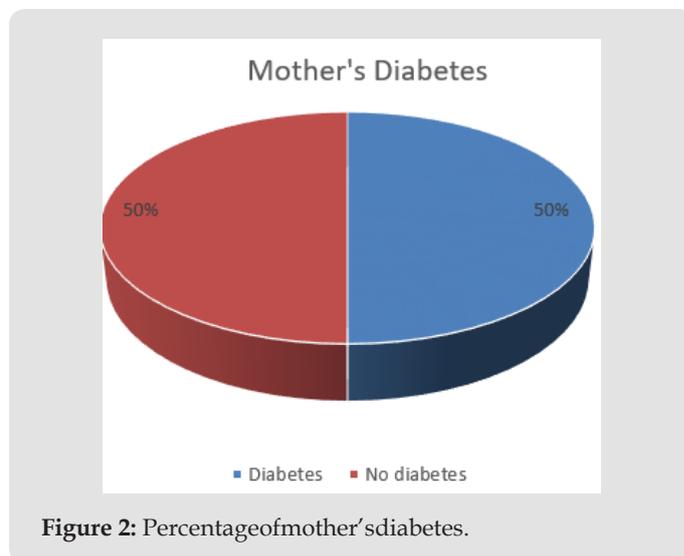
Mother's age	Frequency	Percentage	Average weight	Standard Deviation
18-20 Years	12	15.38	45.4	2.6
21-25 Years	12	15.38	51.2	6.1
26-30 Years	27	34.62	53	5.1
31-42 Years	27	34.62	60.4	7.5
Total	78	100	54.1	7.8

**Mothers' Occupation: Clinical Factors**

It is found that 46% of the mothers were housewife and 22% of them were service holders. About 12% of them were teacher, 6% students and 3% doctor. There were other occupations (10%). Mother's occupation is a valid socio-economic status as it may bring an association of mothers' income status and have more frequently visited a doctor. This also suggests the connection with diabetes and congenital heart disease of children (Figures 1 & 2).



**Figure 1:** Percentage of mother's occupational status.



**Figure 2:** Percentage of mother's diabetes.

**Mother's Diabetes**

To identify any association between the mother's diabetes and the child's CHD, it was assessed that 50% of the mother had diabetes during the pregnancy and the rest 50% didn't had (Fig. 2), only those who suffered from diabetes in recent pregnancy were considered.

**Mothers' Existing Diseases During Pregnancy**

It was found that mothers had different types of diseases during the pregnancy and they had to take medication and it was reported that almost 36 mothers (45%) among 78 had hyperglycemia which means the excess of glucose in the bloodstream. It was found, almost 4% of the mother having hypertension. Almost 5% of the women reported that they had anemia, 3% reported that they had both hyperglycemia and hypertension and 9% had with different other types of diseases. However, 32% of the women were found to have no current disease for which they needed medication (Figure 3).

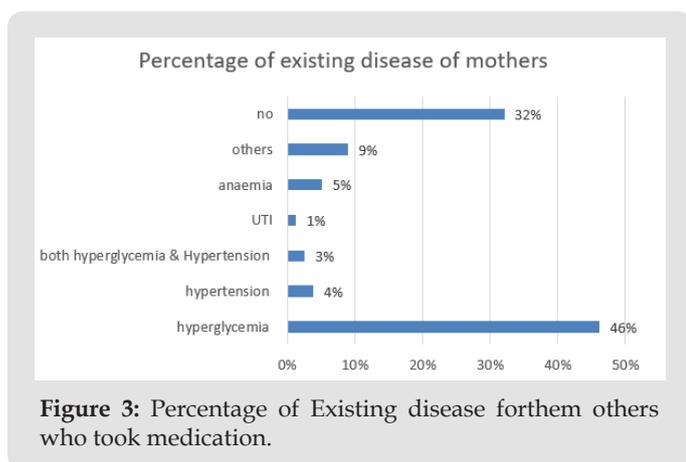


Figure 3: Percentage of Existing disease for them others who took medication.

### Types of Cardiac Problem by CHD Status

While investigating whether the child had Congenital Heart Disease (CHD) or not, based on the test result, it was found that among the CHD patients, 70% of them were affected by the respiratory problem, and 11% of them had distress during the observation. However, it was also found that 5% of the cases where the child had a respiratory problem but was not conclusive to have CHD status. On the contrary, 19% of the children found without any respiratory problem but was detected as CHD patients as they had other complications rather than the respiratory problem (Figure 4).

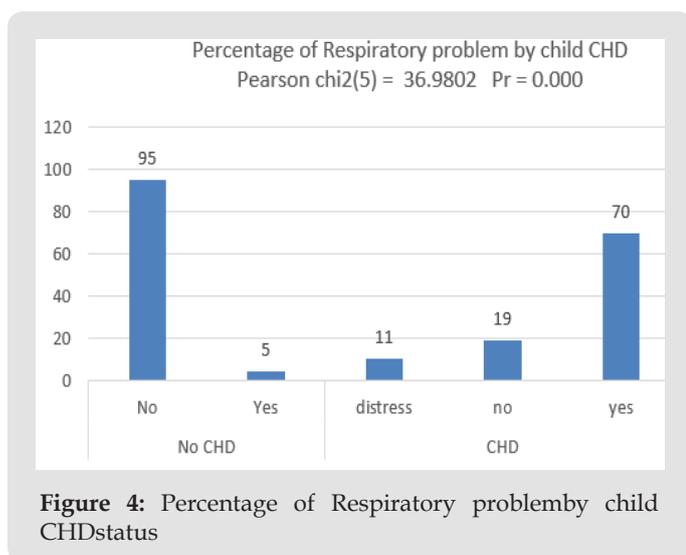


Figure 4: Percentage of Respiratory problem by child CHD status

The analysis compared the types of Cyanosis problem by child CHD status, it was found that 24% of the children had no Cyanosis and were not detected as CHD patient and 4% had no Cyanosis but were detected as CHD. It was found that CHD patients had more problems with the peripheral and both peripheral and central cyanosis than the non-CHD patients. It reveals that CHD patients had more exposure to the cyanosis problem than non-CHD patients. The statistical difference of percentage of cyanosis between the CHD and non-CHD was significant as the Pearson Chi-square test value was above the critical value label and the p-value was less than 5% level (Figures 5 & 6): Percentage of Resuscitation by child CHD status (Table 3).

Table 3: Percentage of Co-existing disease of mothers during the pregnancy.

Types of disease	Frequency	Percentage
UTI	30	38%
Anaemia	20	26%
Hypothyroid	6	8%
Renal disease	2	3%
Preeclampsia	1	1%
DM	1	1%
Hypertension	1	1%
Others	2	3%
No Disease	15	19%
Total	78	100%

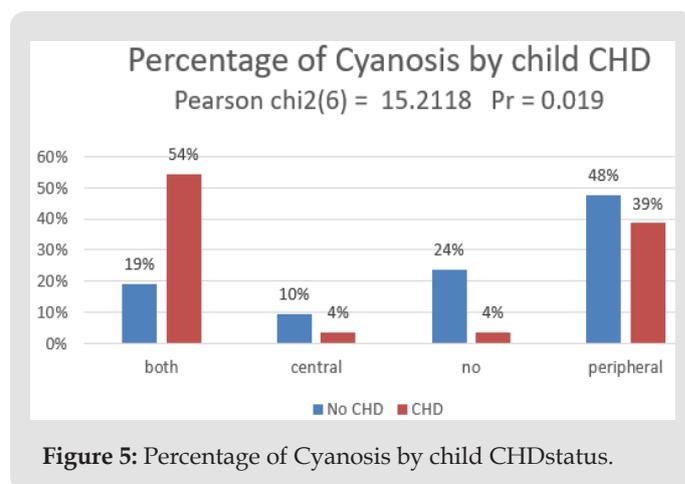


Figure 5: Percentage of Cyanosis by child CHD status.

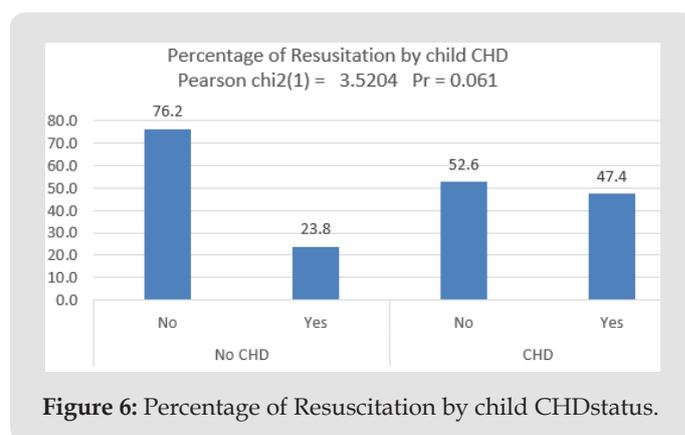


Figure 6: Percentage of Resuscitation by child CHD status.

### The Percentage of Resuscitation by Child CHD

It is found that the percentage of resuscitation was higher in the CHD affected children than those of the non-CHD children. Almost 24% of the resuscitation cases were not detected as CHD problem in the children (Figure 7). The percentage of resuscitation was higher in the CHD affected children than those of the non-CHD children. Almost 24% of the resuscitation cases were not detected as CHD problem in the children. The interaction of the mother's diabetes and the child heart disease showed a significant relationship exists between these two factors. Child CHD was highly

correlated with the mother's diabetes representing 87.18% of the diabetic mothers' children were affected by CHD. Diabetic mothers had more tendencies to have PDA children. Moderate and tiny PDA cases, diabetic mothers had a higher percentage of PDA than other PDA cases. Almost 64% of diabetic mothers had PDA affected children than non-diabetic mothers. It was found that the child ASD cases were positively correlated with the mother's diabetes. In case of mild, moderate, and large ASD cases, the diabetic mothers had higher exposure rate than the non-diabetic mothers (Figure 8).

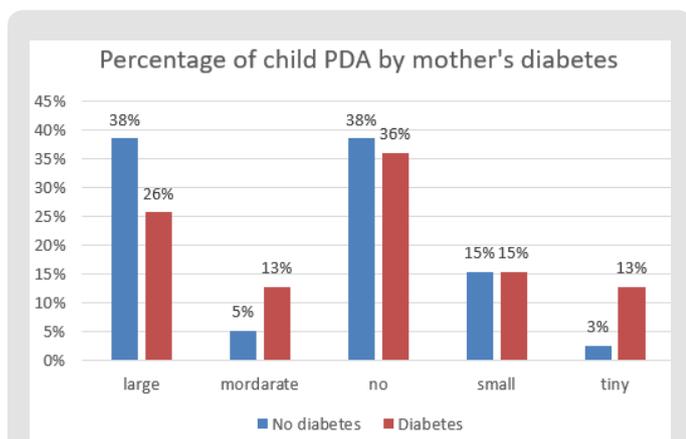


Figure 7: Percentage of Child PDA by mother's diabetes status.

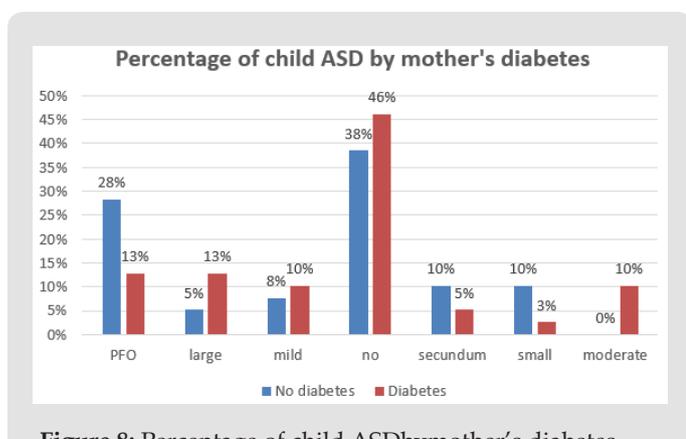


Figure 8: Percentage of child ASD by mother's diabetes.

**Mothers' Co-Existing Diseases During Pregnancy**

Mothers had also some previous existing diseases that the also reported. In most of the cases that most mother had both current and pre-existing diseases during the prepregnancy. One of the topmost co-existing diseases is the UTI and anaemia. It is reported that almost 38% of the women have UTI and 26% of the women had anaemia. Most of the women have this hyperglycemia and UTI and/or anaemia. Besides, 8% of them had hypothyroidism and 3% of them had renal disease. The co-existing diseases found very low diabetes counts and hypertension, which was most possible that those are mentioned in (Figure 3) for which the mother is already taking medicine.

**Congenital Heart Disease Among the Neonate of Diabetic Mothers**

Mother's diabetes and child CHD: The interaction of the mother's diabetes and the child heart disease, there exists a significant relationship between these two factors. Child CHD was highly correlated with the mother's diabetes. It was found that 87.18% of diabetic mothers' children were affected by CHD. 12.82% of the mothers although having diabetes, their children were not affected by CHD. On the other hand, 59% of the non-diabetic mothers' children were having CHD. The Pearson Chi-square test was significant (P<1%) which showed a significant association between the child CHD and mother's diabetes (Table 4).

Table 4: Association of Child Congenital Heart Disease (CHD) and mother's diabetes.

Mother's Diabetes	Congenital Heart Disease (CHD)		
	No	Yes	
No	16	23	39
	-41.03	-58.97	-100
Yes	5	34	39
	-12.82	-87.18	-100
Total	21	57	78
	-26.92	-73.08	-100

Pearson chi2(1) = 7.8847 Pr = 0.005

**Mother's Diabetes Status and the Child Cardiac Problem**

The diabetic mothers had more tendencies to have PDA children according to the (Figure 7). Moderate and tiny PDA cases, the diabetic mothers had higher percentage of PDA than other PDA cases. Almost 64% of the diabetic mothers had the PDA affected children than the non-diabetic mothers. In the current study, PPHN and PDA were found to be the commonest CHD which was followed by ASD and VSD (Figure 9). However, this study has found that the PPHN (82%) and PDA (70%) is higher than any other studies mentioned here possibly because of the neonates who were admitted into the hospital and had these issues.

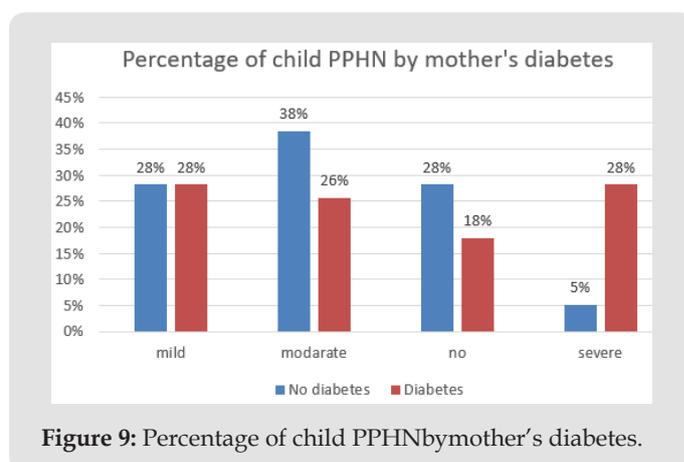


Figure 9: Percentage of child PPHN by mother's diabetes.

### Regression Results

The study applied logistic regression model as the outcome variable was binary in nature (CHD=1, or 0). The presented odds ratio showed the likelihood of occurring the event due to the other independent variables. The study hypothesized that CHD is a function of the mother’s characteristics and household characteristics. There is a statistically significant association present between the CHD of neonatal children (within 28 days of age) and the mother’s diabetes. It shows that if the mother had GDM (diabetes) then the probability of having CHD of the neonate increases by 5.8 times higher than a non-diabetic mother which is significant at 5% level. Mother age was also found significantly associated with the CHD of the child. It shows that the aged mother tends to have the child with CHD 1.14% higher than a young aged

mother which is significant at 10% level of significance. Mother’s weight is also found to have a significant negative association with the CHD of the child at 5% level of significance. It implies that mothers with higher weight tend to have non-CHD babies than the lower-weight mother counterpart. Mothers having unwanted event before the current pregnancy possess a significant positive association with the CHD of the child. It implies that if there is presence of unwanted event before the current pregnancy among the mothers, the probability of CHD among the neonatal babies increases by 4.3 times which is significant at 10% level. All these results are controlled for all other variables such as family income, the number of pregnancies, the record of family hypertension, birth trimester, mother’s doing exercise, weight of child, and correction of diabetes of mother etc. (Table 5).

**Table 5:** Logistic Regression Results.

CHD	Odds ratio	St.Err.	t-value	p-value	[95% Conf	Interval]	Sig
Mother diabetes	5.842	5.178					
1.99	0.046	1.028	33.194	**			
Mother age	1.136	0.085	1.71	0.086	0.982	1.315	*
Family income	1	0	0.9	0.369	1	1	
Mother’s weight	0.875	0.057	-2.05	0.04	0.77	0.994	**
Number of pregnancies	0.793	0.268	-0.69	0.492	0.409	1.538	
Unwanted event	4.288	3.57	1.75	0.08	0.838	21.928	*
Hypertension family	0.817	0.655	-0.25	0.801	0.17	3.932	
Birth trimester	0.909	0.071	-1.22	0.222	0.78	1.059	
Mother’s exercise	1.703	1.204	0.75	0.452	0.426	6.809	
Weight of child	1	0.001	0.32	0.746	0.999	1.001	
Correction of diabetes	1.376	1.031	0.43	0.67	0.317	5.977	
Constant	279.9	968.2	1.63	0.103	0.318	246350	
Mean dependent var	0.731		SD dependent var		0.446		
Pseudo r-squared	0.22		Number of obs		78		
Chi-square	20.026		Prob> chi2		0.045		
Akaike crit. (AIC)	94.843		Bayesian crit. (BIC)		123.123		

\*\*\*p<0.01, \*\* p<0.05, \* p<0.1

### Discussion

Congenital heart disease among the neonatal children was identified the types of CHD problems. The incidence varies from locality, region, exposure areas, and even the countries, however most countries reported it to be 4/1000 to 50/1000 live birth [20]. Many studies also reported that it is increasing globally as well as in Bangladesh [17,18]. However, in Bangladesh there is no nationwide study on that however, different studies suggest that the incidence of CHD in Bangladesh is around 18/1000. Literature has reported that the causes of CHD is multifaceted and multidimensional and results from a mixture of inherited predilection and environmental impetus. Similar study was conducted at the Joslin et al in 1973 identifying a fivefold risk of CHD of neonate children of the DM

mothers than the non-DM mothers. The present investigation is based on the conceptual analysis where it outlined that neonatal congenital heart disease is linked with mother’s characteristics, socioeconomic characteristics of the family, mother’s disease profile such as records of diabetes, hypertension, hypothyroidism, anemia, and UTI, and child characteristics such as child weight, pregnancy delivery weeks (trimester) etc. Mother’s hypertension, hypothyroidism and diabetes and anaemia also possess a great risk towards the neonatal CHD. Mother’s occupation was a valid socio-economic status as it might bring an association of mothers’ income status and having more frequently visited a doctor.

Early delivery of pregnancy could be one of the reasons for CHD. It was found that most women had their deliveries at the week of

37. It was not surprising that few women (almost 5%) had delivery before they reach at 28 weeks. This type of early delivery of the baby causes congenital heart disease found in the literature. About 14% of the mother had their child delivery before 32 weeks of their pregnancy; however, almost 5% told that they have late deliveries of their babies. In the neonatal outcome, birth weight is one of the important characteristics of CHD. It was found that almost 58% of the sample size was born with low birth weight meaning less than 2.5 kg which was an alarming signal. Only 30% of the sample babies were born with being 2.5 to 3kg. So, in total it can be said that almost 86% of the sample babies in this study was less than 3 kg when at birth. This is a clear indication that they would have other complication later their life. A Healthy baby should have a good birth weight (more than 2.5kg).

In the current study, PPHN and PDA were found to be the commonest CHD which was followed by ASD and VSD. These findings differs with the findings of but similar to. This study found that acyanotic CHD was the commonest heart disease which was also similarly found in many other studies ASD (67%) and VSD (25%) were found in the study complies with other studies such as. However, this study has found that the PPHN (82%) and PDA (70%) is higher than any other studies mentioned here possibly because of the neonates who were admitted into the hospital and had these issues. It is also found that many neonatal had multiple lesion which also confirmed by other studies such as.

Comparing the types of Cyanosis problem by child CHD status, it has found that 24% of the children had no Cyanosis and was not detected as CHD patient and 4% had no Cyanosis but were detected as CHD. CHD patients had more problems with the peripheral and both peripheral and central cyanosis than the non-CHD patients. It revealed that CHD patients had more exposure to the cyanosis problem than non-CHD patients. The statistical difference of percentage of cyanosis between the CHD and non-CHD was significant. The regression result showed that there was a statistically significant association present between the CHD of neonatal children and the mothers' diabetes. This result is similar to the results found in [21]. It showed that if the mother had GDM (diabetes) then the probability of having CHD of the child increases by 5.8 times higher than a non-diabetic mother which was significant at 5% level. This result is similar to the studies of Where Archives of Disease in Childhood (ADC) have found DM increased the CHD by 5 times, found this relationship of DM increased the CHD by 4 times. [22] discussed the mother's diabetic factor as a underlying cause, but didn't identify the impact of it on CHD. The Mother age also found significantly associated with the CHD of the child. It showed that the aged mother tends to have a child with CHD 1.14% higher than a young aged mother which was significant at 10% level of significance.

## Conclusion and Recommendation

The present investigation identified that, the association between the neonatal congenital heart diseases and the mother's diabetic status based on some clinical and observational data from 78 randomly selected patients who got admitted to the Intensive Care Unit (ICU) during the study period. The sample was random because the researcher didn't have any control who would come for the admission and who will not. The sampling was completely random. This result shows that there was a positive association among CHD and mother's diabetes, age, and having unwanted events. On the other hand, the mothers' weight had a negative relationship with the CHD of children. This study identifies the association between the neonatal congenital heart diseases and the mother's diabetic status based on some clinical and observational data from 78 randomly selected patients who got admitted to the Intensive Care Unit (ICU) during the study period.

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