The Professional Medical Journal
www.theprofesional.com

DOI: 10.29309/TPMJ/2020.27.05.3924

ORIGINAL PROF-0-3924

CONGENITAL HEART DEFECTS IN INFANTS BORN TO DIABETIC MOTHER (IDM): A SINGLE CENTER EXPERIENCE.

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Article received on:
09/07/2019
Accepted for publication:
15/10/2019

ABSTRACT: Neonates born to diabetic mothers are more prone to develop congenital anomalies and defects. Overall risk of development of congenital malformations increases by 2-12% compared to normal neonates. In Pakistan, the true prevalence of CHD is unknown. **Objectives:** To determine the frequency of congenital heart diseases in infants born to diabetic mothers (IDM). **Study Design:** Cross Sectional Study. **Setting:** Department of Pediatrics, Allied Hospital, Faisalabad. **Period:** Six month, August 16, 2017 to February 16, 2018. **Material & Methods:** Total 295 neonates born to diabetic mothers diagnosed presenting in neonatal unit were enrolled in study. Chest X-ray, electrocardiography (ECG) and echocardiography were done to identify CHDs. **Results:** Total 292 infants born to diabetic mother were selected. Mean age of the patients was 10.1±5.9 days. Of total, 189 (64.7%) were males and 103 (35.3%) were females. Out of 292 infants of diabetic mothers, 138(47.3%) were having various (CHD) and remaining 48(47.5%) were found normal after echocardiography. **Conclusion:** The cardiovascular system along with other systems of the body of neonates is affected in about 50% of the neonates born to diabetic mothers. Early diagnosis of CHD using a screening echocardiography is recommended to morbidity and mortality.

Key words: Congenital Heart Diseases, Diabetic Mothers, Gestational Diabetes Mellitus, Pre-Gestational Diabetes Mellitus.

Article Citation: Shamaoon M, Zunaira, Ahsan M, Maqbool T, Aslam R, Yaseen A. Congenital heart defects in infants born to diabetic mother (IDM): A single center experience. Professional Med J 2020; 27(5):950-956.
DOI: 10.29309/TPMJ/2020.27.05.3924

INTRODUCTION

Congenital cardiovascular defects are one of the prevalent groups of birth anomalies; roughly affecting 6–8 babies per 1000 live births. Cause is usually not known but some are genetic while few have an environmental etiology. About 1 out of 100 of these cases is due to some maternal disease.[1]

In Europe, while estimating the causes of neonatal mortality, 10.4% of these infants had a congenital heart disease. It was seen that neonatal mortality rate decreased due to increasing termination of pregnancy and survival after cardiac surgeries.[2]

Infants of diabetic mother (IDM) babies are more prone to develop congenital anomalies and defects. Overall risk of development of congenital malformations increases by 2-12% compared to normal neonates, most frequent being the congenital heart disease (CHD) and poly-malformation syndrome.[3-5]

Maternal diabetes is known to have teratogenic effects during 1st trimester during the development of heart. Cardiovascular malformations are more in infants of diabetic mothers (IDM) as compared to babies with non-diabetic mothers.[1-2,4]

Frequency of congenital heart disease (CHD) in IDM babies is about 5%. Most frequent ones are ventricular septal defect (VSD), transposition of great arteries (TGA), aortic stenosis, truncus arteriosus and double outlet right ventricle.[5]

Abu-sulaeiman RM. reported the frequency of patent ductus arteriosus (PDA; 70%), patent foramen ovale (PFO; 68%), atrial septal defect

(ASD; 5%), hypertrophic cardiomyopathy (HCMP; 38%).[6]

Muhammad A. reported the frequency of PDA 16.8%, VSD 12.9%, ASD 8.9%, patent foramen ovale (PFO) 7.9% and TGA 5.9% in IDM neonates.[7] Ferdousi S. also reported the frequencies of patent Foramen Ovale (60.71%), PDA 55.3%, hypertrophic Cardiomyopathy (21.42%) and ASD (10.71%) in IDM babies in Bangladesh.[8] The aim of this study was to know the frequency of congenital heart diseases in infants born to diabetic mothers.

MATERIAL & METHODS

This cross sectional study included patients from pediatric Ward, emergency and OPD of Allied Hospital, Faisalabad during August 16, 2017 to February 16, 2018 through Non-probability consecutive sampling technique. All full term neonates of 0 to 30 day of life of both genders born to diabetic mother according to operational definition of age less than 35 years were included in the study. Infant of diabetic mother was defined as an infant born to mother having diabetes previously or during pregnancy with fasting blood sugar > 126mg/dL and random blood sugar > 200 mg/dL confirmed by glucose tolerance test (after 75g sugar intake RBS > 200mg/dL after 1 hour and RBS > 140mg/dL after 2 hours).

Congenital Heart diseases was defined as ayanotic and acyanotic congenital heart diseases confirmed on echocardiography including PDA, VSD, ASD, PFO, TGA and tetralogy of fallet (TOF). Any patent was labeled to have PDA if Doppler echocardiographic shows left right ductal shunt with any two of the following: heart murmur (systolic or continuous); tachycardia (heart rate persistently more than 160/min); hyperactive precordial pulsation; bounding pulses; and radiographic evidence of cardiomegaly or pulmonary congestion. PFO with ASD was confirmed when the presence of a shunt is demonstrated with color flow in the 2-dimensional views of the fossa ovalis without drop-out, or when a tiny flap-like septum primium was detected in the left atrium and the septum secundum was seen in the right atrium in the presence of canal-type defect. Patency of less than 3 mm around the fossa ovalis is called PFO if it is more than 3 mm, and was considered to be an ASD. VSD was defined as any patient having pansystolic murmur with a defect seen in the ventricular septum and left right shunting. Transposition of Great Arteries (TGA) in Neonates having cyanosis on clinical examination and egg on string appearance on chest x-ray reported by consultant radiologist and ECHO showing abnormal anatomical structures i.e aorta and pulmonary trunk without any connection or cross was labeled as TGA. Tetralogy of Fallot (TOF) in neonates having cyanosis on clinical examination and boot shaped heart appearance on digital radiography reported by consultant radiologist and echo showing abnormal anatomy including ventral septum defect (VSD), right ventricular outflow tract (RVOT) obstruction, overriding of the aorta and right ventricular hypertrophy was labelled as TOF. In hypertrophic cardiomyopathy (HOCM): Echocardiography showing left ventricular (LV) wall thickness of more than or equal to 15 mm at end-diastole or a septal-to-lateral-wall thickness ratio more than 1.3 in a non-dilated LV in the absence of a loading condition was diagnosed as HOCM.

Known cases of congenital heart disease, premature <37 weeks or those with CNS or pulmonary anomaly or those having severe hypoxia or neonatal sepsis along with those born to mothers with history of hypertension, chronic kidney disease, hepatitis, heart failure, tuberculosis, preeclampsia, rheumatic-heart-disease or drugs intake except insulin for diabetes were excluded. Sample Size of 292 was calculated using WHO sample size calculator, with confidence level of 95%, absolute precision 2.5% and p = 5%.[5] Demographic details like age, gestational age at birth, gender and relevant data according to the predesigned questionnaire were documented. Antenatal record of mother was assessed for gestational diabetes mellitus. Detailed examination to pick any cardiac and extra-cardiac abnormalities was done. Chest X-ray, electrocardiography (ECG) and echocardiography were done. Echocardiography was done by experienced pediatric cardiologist

in Faisalabad Institute of Cardiology using 2D colour Doppler in M mode. Results of all the investigations were documented.

The data were analyzed using SPSS v23.0. Qualitative variables including gender, presence of cyanosis, presence of ASD, VSD, TGA, TOF, PDA, PFO, type of DM and congenital heart disease were analyzed and frequency was calculated along with percentage. For the quantitative variables like age, weight, gestational age at birth and RBS at birth, mean ± S.D was computed. Effect modifiers like age, type of DM, birth weight, gestational age and gender of the patient were stratified to find out the effect of these on the outcome, through chi square ($p<0.05$ was considered significant).

RESULTS

Total 292 infants born to diabetic mother were selected for this study. Mean age of the patients was 10.1±5.9 days. Total 189(64.7%) were males and 103(35.3%) were females.

Age distribution of the patients was done and two groups were made, age group 0-10 days and age group 11-20 days. 156(53.4%) patients were in age group of 0-10 days. 136(46.6%) were in 11-20 days age group.

According to type of diabetes mellitus, 164(56.2%) mothers had gestational diabetes mellitus and 128(43.8%) had pre-gestational DM. 179(61.3%) infants were in 37-39 weeks of gestational age and 113(38.7%) were in 39-42 weeks.

Among these infants, 7(2.4%) had cyanosis at birth. 176(60.3%) had 2500-3500 grams weight at birth, while 116(39.7%) had >3500 grams.

Out of 292 infants of diabetic mothers, 138(47.3%) were diagnosed to have any CHD and remaining 48(47.5%) were found normal after echocardiographic examination.

Following CHD were found in 138 infants of diabetic mothers; Patent ductus arteriosus (PDA) in 45(32.6%) cases, Ventricular septal defect (VSD) in 35(25.3%) cases, Atrial septal defect (ASD) in 20(14.5%), Patent foramen ovale (PFO) in 15(10.8%), Transposition of the great arteries (TGA) in 11(7.9%) cases, Hypertrophic Cardio Myopathy (HCM) in 8(5.7%) cases and Tetralogy of Fallot (TOF) in 4(2.8%) cases.

Type of Diabetes Mellitus	Frequency	Percent
Gestational	164	56.2
Pre-Gestational	128	43.8
Total	292	100.0

Table-I. Frequency distribution of type of diabetes mellitus.

Gestational Age at Birth	Frequency	Percent
37-39 weeks	179	61.3
39-42 weeks	113	38.7
Total	292	100.0

Table-II. Frequency distribution of gestational age at birth.

Cyanosis at Birth	Frequency	Percent
Yes	7	2.4
No	285	97.6
Total	292	100.0

Table-III. Frequency distribution of cyanosis at birth.

Weight at Birth	Frequency	Percent
2500-3500 grams	176	60.3
≥3500 grams	116	39.7
Total	292	100.0

Table-IV. Frequency distribution of weight at birth.

Chd	Frequency	Percent
Patent ductus arteriosus (pda)	45	32.6
Ventricular septal defect (vsd)	35	25.3
Atrial septal defect (asd)	20	14.5
Patent foramen ovelo (pfo)	15	10.8
Transposition of the great arteries (tga)	11	7.9
Hypertrophic cardiomyopathy (hcm)	8	5.7
Tetralogy of fallot (tof)	4	2.8
Congenital heart disease	138	47.3

Table-V. Frequency distribution of various congenital heart diseases (CHD).

Gender	Congenital Heart Disease		Total	P-Value
	Present	Absent		
Male	89	100	189	0.937
	47.1%	52.9%	100.0%	
Female	49	54	103	
	47.6%	52.4%	100.0%	
Total	138	154	292	
	47.3%	52.7%	100.0%	

Table-VI. Stratification of congenital heart disease with respect to gender.

Age Groups	Congenital Heart Disease		Total	P-Value
	Present	Absent		
0-10 days	71	85	156	0.522
	45.5%	54.5%	100.0%	
11-20 days	67	69	136	
	49.3%	50.7%	100.0%	
Total	138	154	292	
	47.3%	52.7%	100.0%	

Table-VII. Stratification of congenital heart disease with respect to age.

Type of Diabetes Mellitus	Congenital Heart Disease		Total	P-Value
	Present	Absent		
Gestational	73	91	164	0.287
	44.5%	55.5%	100.0%	
Pre-Gestational	65	63	128	
	50.8%	49.2%	100.0%	
Total	138	154	292	
	47.3%	52.7%	100.0%	

Table-VIII. Stratification of congenital heart disease with respect to type of diabetes mellitus.

Gestational Age at Birth	Congenital Heart Disease		Total	P-Value
	Present	Absent		
37-39 weeks	89	90	179	0.289
	49.7%	50.3%	100.0%	
39-42 weeks	49	64	113	
	43.4%	56.6%	100.0%	
Total	138	154	292	
	47.3%	52.7%	100.0%	

Table-IX. Stratification of congenital heart disease with respect to gestational age at birth.

Weight at Birth	Congenital Heart Disease		Total	P-Value
	Present	Absent		
2500-3500 grams	81	95	176	0.602
	46.0%	54.0%	100.0%	
≥3500 grams	57	59	116	
	49.1%	50.9%	100.0%	
Total	138	154	292	
	47.3%	52.7%	100.0%	

Table-X. Stratification of congenital heart disease with respect to weight at birth.

DISCUSSION

Any pregnancy mother having diabetes before conceiving or having gestational diabetes makes the pregnancy at a serious risk, especially those with type 1 diabetes.[9-11] Reason being that studies have shown that fetuses of type II DM patients are prone to development of such complications induced by uncontrolled blood sugar.[12-15]

Neonates born to mothers with maternal diabetes mellitus (MDM) have an estimated increased risk of development of CHD of up to 8.5%. Structural abnormalities from setal defects to duct-dependent lesions are seen in IDM.[24-25]

We found that in our study CHDs were seen in 138 infants of diabetic mothers; these include PDA 45 (32.6%) cases, VSD 35 (25.3%) cases, ASD 20 (14.5%), PFO 15 (10.8%), TGA 11 (7.9%) cases, HCM 8 (5.7%) cases and TOF in 4 (2.8%) cases. Similar results have been reported by many other local and international studies, few differences in frequencies can be due to difference in sample sizes and study duration. Our study was limited to 6 months period.

Hussain M, et al reported that only about 5% (2/42) IDM were diagnosed to have any CHD.[16] Behjati M, et al reported this to be 9.3% (but he excluded PDA and hypertrophic cardiomyopathy).[17] but we reported about 47.3% of the IDM children were diagnosed with CHD. This is an alarmingly high percentage of affected IDM patients; it can be due to a small sample size of our study as it was a single center study.

Hussain M, et al reported that in his study, 29 (69%) IDM patients were male and 13 (31%) were females, with a ratio of male gender with female gender of 2:1.[16] Masood N, et al reported after a survey on about ten thousand neonates, with 96 (about 10%) were diagnosed having CHD; 64 male and 32 female, ratio of 2:1).[19] Similar results were also found in our study where majority (64.7%) was males and (35.3%) were females. Male preponderance has been reported by many other studies as well.[20-22] In Hazara, Burki NM, et al reported that the frequency of IDM children with CHD was almost same in both genders.[23]

Behjati M, et al in his study showed that CHD was more common among the neonates of pre-gestational diabetes as compared to those born to mothers with gestational DM (49 (65%) and 36 (35%), respectively).[17] But, Aslam M, et al reported that gestational diabetes was in 75% patients and pre-gestational diabetes in 25% patients.[18] In our study, more than fifty percent (56.2%) of the patients were of mothers with gestational diabetes whil 43.8% had pre-gestational diabetes.

In a study, PDA was seen among 17% cases, pulmonary stenosis 6%, and hypertrophy of the ventricular septum 33.8% cases.[26] In another study common structural cardiac lesions were PDA in 54.7% cases, HCMP 24%, VSD in 4%, ASD 2.7%, TGA and COA in 1.3% cases each.[17]

A study of Lahore, Pakistan surveyed 1530 full-term newborns, 6% were IDMs, and congenital anomalies were seen in 13% of these cases CHD being the most common anomaly.[18]

Abu-Sulaiman RM, et al from Saudi Arabia reported that PDA was seen in 70% cases, PFO in 68%, ASD in 5%, small muscular VSD in 4%, mitral valve prolapse in 2%, and PS 1% case respectively.[27] Korraa A, et al reported that asymmetrical septal hypertrophy in 80%, PFO in 37.5%, and PDA in 27.5% cases of IDM.[28]

At this, we concluded that the earlier you detect the cardiac lesions, easier it is to manage these patients and complications associated, thus preventing morbidity and improving survival. For this purpose every newborns, especially those at risk of development of CHD should be examined in the neonatal units and post-natal stabilization units and even in the vaccination centers and primary health care units.[20]

CONCLUSION

The cardiovascular system along with other systems of the body of neonates is affected in about 50% of the neonates born to diabetic mothers. Early diagnosis of CHD using a screening echocardiography is recommended to morbidity and mortality.

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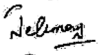
4	Tehmina Maqbool	Data analysis, Paper writing.	
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