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Spectrum of Congenital Heart Diseases in Infant of Diabetic Mother in NICU of Tertiary Care Hospital

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Abstract: Background: Infants of diabetic mothers (IDMs) are at increased risk of congenital heart diseases CHDs due to maternal hyperglycemia affecting fetal cardiac development. **Objective:** To determine the frequency and spectrum of CHDs in IDMs and evaluate the role of echocardiography in early diagnosis. **Methodology:** This descriptive cross-sectional study was conducted in the Department of Pediatrics, Benazir Bhutto Hospital, Rawalpindi, over six months from April to September 2023. A total of 150 neonates born to diabetic mothers were enrolled using consecutive sampling. Infants aged 0–28 days with gestational age 35–40 weeks were included. Data regarding demographic and clinical characteristics were collected, and all neonates underwent echocardiographic evaluation. Statistical analysis was performed using SPSS version 23, and results were expressed in frequencies and percentages. **Results**: Out of 150 infants, congenital heart disease was detected in 113 (75.33%), while 37 (24.67%) had normal echocardiography findings. The most common lesions included patent ductus arteriosus in 42 (28.00%), ventricular septal defect in 16 (10.67%), atrial septal defect in 12 (8.00%), and septal hypertrophy in 19 (12.67%). Transposition of great arteries was observed in 6 (4.00%) and tetralogy of Fallot in 3 (2.00%) cases. Echocardiography was performed within 24 hours in 118 (78.67%) neonates, and both symptomatic CHD in 77 (51.33%) and asymptomatic CHD in 36 (24.00%) cases were identified. No significant association was found between CHD and neonatal age, gender, maternal age, mode of delivery, or birth weight ($p>0.05$). **Conclusion:** The study demonstrates a high frequency of CHDs in IDMs, with echocardiography playing a crucial role in early detection.

Keywords: Infants of diabetic mothers, congenital heart disease, echocardiography, neonatal intensive care unit, cardiac anomalies.

INTRODUCTION

Diabetes mellitus in pregnancy, which is maternal diabetes mellitus (DM), is one of the most frequently occurring metabolic diseases of pregnancy, and is linked to higher rates of perinatal morbidity [1]. Infants of diabetic mothers (IDMs) are especially prone to multiple problems such as respiratory distress, hypoglycemia, macrosomia, prematurity, metabolic disturbances, and congenital anomalies [2]. One of the most serious and clinically important complications encountered in neonatal intensive care units (NICUs) is congenital heart diseases (CHDs) [3]. The rates of congenital malformations are significantly increased in IDMs as compared to infants born from non-diabetic mothers, especially heart defects which are the most commonly reported structural anomalies [4].

Fetal heart development takes place in the early weeks of gestation when maternal hyperglycemia can impact on embryogenesis [5]. The impairment of glycaemic control during organogenesis has been associated with abnormal cardiac morphogenesis, and a higher risk of cardiac structural and functional abnormalities [6]. The most frequent CHDs are ventricular septal defect (VSD), atrial septal defect (ASD), transposition of great arteries, patent ductus arteriosus (PDA), and hypertrophic cardiomyopathy [7]. These

abnormalities can have clinical presentations that vary in severity from being asymptomatic with a murmur, to a more severe presentation that may result in severe cyanosis and heart failure, which may require intensive neonatal management [8].

Neonatal outcome of IDMs is also related to birth weight [9]. The macrosome and low-birth-weight babies can have different patterns of cardiovascular complication, because of the difference in intrauterine metabolic conditions [10]. Infants with macrosomia due to fetal hyperinsulinism often have cardiac hypertrophy while those with growth restriction can have impaired cardiac adaptation postnatally [11]. Thus, evaluation of CHDs in various birth weight groups is important to help understand the babies and guide their management in the first days of life [12].

It is very important to identify CHD in IDMs early and decrease neonatal morbidity and clinical outcomes. Echocardiography has proven to be a valuable, non-invasive and very sensitive method for detecting cardiac abnormalities in the early stages of life in neonates. In the NICU environment, an early echocardiographic screen allows for efficient diagnosis and timely treatment of the patient, especially when the infant is born to a diabetic mother.

Research Objective

To ascertain the frequency and type of congenital heart disease in IDMs having different birth weight and use of echocardiography in early diagnosis.

METHODOLOGY

Study Design and Setting

This descriptive cross sectional study was carried out in the Department of Paediatrics at Benazir Bhutto Hospital, Rawalpindi Medical University and its allied hospitals. The study comprised IDMs admitted to NICU for evaluation of CHD by echocardiography.

Study Duration

This study was conducted for six months starting from 1st April 2023 to 30th September 2023.

Sample Size and Sampling Technique

Sample size was estimated by WHO sample size calculator and was determined as 150 patients. The frequency of CHDs in IDMs was obtained and reported as 52.5% and anticipated population proportion was 0.525, a 95% confidence level and an absolute precision of 8%. Participant recruitment was done using a probability consecutive sampling technique.

Inclusion and Exclusion Criteria

This study comprised neonates born to mothers with either gestational diabetes mellitus or pregestational diabetes mellitus, within the age range of 0-28 days and gestational age of between 35 and 40 weeks. Low birth weight, normal birth weight and large for gestational age (LGA) were also used to classify the IDMs based on birth weight. Neonates with concomitant complications (including sepsis and birth asphyxia) or gestational age less than 35 weeks were excluded.

Data Collection Procedure

Data were collected from the department of Pediatric Medicine, Benazir Bhutto Hospital, Rawalpindi Medical University and Allied Hospitals. All eligible neonates admitted to the NICU were consecutively enrolled irrespective of mothers' gestational or pregestational diabetes mellitus. A special designed proforma was completed for demographic and clinical information such as gestational age, mode of delivery, birth weight, maternal diabetics status and age, gender. Infants were classified into low birth weight (LBW), normal birth weight (NBW), and large for gestational age (LGA). Clinical features suggestive of CHD were recorded. Infants were evaluated by a pediatric cardiologist with an echocardiogram, both if they were found to be sick, and if they did not show any signs of illness. The echocardiographic findings and other clinical details were systematically documented.

Statistical Analysis

All the collected data were fed and processed in the Statistical Package for Social Sciences (SPSS) version 23.0. The quantitative variables, birth weight and age at presentation, were presented as mean and standard deviation. Frequencies and percentages were used to present qualitative variables such as gender, clinical presentation and types of CHDs. Chi-square test was used to evaluate the effect of potential modifiers (neonatal age, maternal age, gender, mode of delivery and birth weight) on the frequency of CHD. Statistically significance was considered with p value < 0.05.

Ethical Consideration

The study was approved by the institutional ethical review committee and the synopsis was approved by the College of Physicians and Surgeons Pakistan (CPSP). This study was carried out in Department of Pediatrics, Benazir Bhutto Hospital with CPSP Registration Number PED-2020-126-5857 from 26-02-2020 onwards under supervision. Parents/carers of all participants gave written informed consent and confidentiality of patient information was assured throughout the study.

RESULTS

Out of 150 IDMs, most were aged ≤14 days (97, 64.67%) with a mean age of 12.42±6.96 days (table 1). Gender distribution was almost equal, with 74 males (49.33%) and 76 females (50.67%). Most infants were born at ≥37 weeks' gestation (116, 77.33%), and mean gestational age was 37.36±1.21 weeks. Maternal age was predominantly 20–35

years (128, 85.33%) with a mean of 30.92±4.58 years. Majority had birth weight >3.0 kg (124, 82.67%) with mean birth weight of 3.43±0.47 kg, and most were delivered via Caesarean section (119, 79.33%). Clinically, murmur was the most common finding (71, 47.33%) followed by respiratory distress (24, 16.00%), while 39 (26.00%) had no clinical signs. On echocardiography, PDA (42, 28.00%) was most frequent CHD followed by septal hypertrophy (19, 12.67%), VSD (16, 10.67%), PFO (15, 10.00%), ASD (12, 8.00%), TGA (6, 4.00%), TOF (3, 2.00%), and dextrocardia (1, 0.67%), while 36 (24.00%) had normal findings.

Table 1: Demographic, Clinical Characteristics and Types of Congenital Heart Disease in IDMs

Variable	Category	Frequency (n)	Percentage (%)
Age (days)	≤ 14	97	64.67
	15–28	53	35.33
	Mean ± SD	12.42 ± 6.96	
Gender	Male	74	49.33
	Female	76	50.67
Gestational age (weeks)	≤ 36	34	22.67
	≥ 37	116	77.33
	Mean ± SD	37.36 ± 1.21	
Maternal age (years)	20–35	128	85.33
	36–45	22	14.67
	Mean ± SD	30.92 ± 4.58	
Birth weight (kg)	≤ 3.0	26	17.33
	> 3.0	124	82.67
	Mean ± SD	3.43 ± 0.47	
Mode of delivery	SVD	31	20.67
	Caesarean section	119	79.33
Clinical features	Cyanosis	8	5.33
	Respiratory distress	24	16.00
	Murmur	71	47.33
	Low oxygen saturation	5	3.33
	Congestive cardiac failure	3	2.00
	No clinical features	39	26.00
CHD on echocardiography	PDA	42	28.00
	Tetralogy of Fallot	3	2.00
	Transposition of great vessels	6	4.00
	VSD	16	10.67
	Atrial septal defect	12	8.00
	Patent foramen ovale	15	10.00
	Dextrocardia	1	0.67
	Septal hypertrophy	19	12.67
	Normal	36	24.00

Distribution of CHD types across effect modifiers showed that PDA was most frequent in infants ≤14 days (33.00%), in mothers aged 20–35 years (27.34%), females (32.89%), C-section deliveries (29.41%), and infants weighing ≤3.0 kg (50.00%), shown in table 2. VSD was higher in C-section deliveries (11.76%) and normal-weight infants (12.10%), while septal hypertrophy was common in ≥3.1 kg infants (14.52%) and females (14.47%). ASD and PFO were also more frequent in older maternal age (36–45 years) with 13.64% and 22.73% respectively. TOF and dextrocardia were rare across all categories.

Table 2: Association of effect modifiers with different CHDs in IDMs (n = 150)

Effect modifier	Category	PDA n (%)	TOF n (%)	TGA n (%)	VSD n (%)	ASD n (%)	PFO n (%)	Dextrocardia n (%)	Septal hypertrophy n (%)
Infant age (days)	≤14	32 (33.00)	3 (3.10)	5 (5.20)	14 (14.40)	7 (7.20)	13 (13.40)	1 (1.00)	14 (14.40)
	15–28	10 (18.87)	0 (0.00)	1 (1.89)	2 (3.77)	5 (9.43)	2 (3.77)	0 (0.00)	5 (9.43)

Mother age (years)	20–35	35 (27.34)	3 (2.34)	4 (3.12)	13 (10.16)	9 (7.03)	10 (7.81)	1 (0.78)	16 (12.50)
	36–45	7 (31.82)	0 (0.00)	2 (9.09)	3 (13.64)	3 (13.64)	5 (22.73)	0 (0.00)	3 (13.64)
Gender	Male	17 (22.97)	2 (2.70)	4 (5.41)	9 (12.16)	4 (5.41)	10 (13.51)	0 (0.00)	8 (10.81)
	Female	25 (32.89)	1 (1.32)	2 (2.63)	7 (9.21)	8 (10.53)	5 (6.58)	1 (1.32)	11 (14.47)
Mode of delivery	SVD	7 (22.58)	0 (0.00)	1 (3.23)	2 (6.45)	4 (12.90)	5 (16.13)	0 (0.00)	4 (12.90)
	C-section	35 (29.41)	3 (2.52)	5 (4.20)	14 (11.76)	8 (6.72)	10 (8.40)	1 (0.84)	15 (12.61)
Birth weight (kg)	≤3.0	13 (50.00)	1 (3.85)	2 (7.69)	1 (3.85)	2 (7.69)	2 (7.69)	0 (0.00)	1 (3.85)
	≥3.1	29 (23.39)	2 (1.61)	4 (3.23)	15 (12.10)	10 (8.06)	13 (10.48)	1 (0.81)	18 (14.52)

Overall, congenital heart disease was present in 113 (75.33%) infants and absent in 37 (24.67%), shown in table 3. CHD prevalence was similar across age groups (≤14 days: 75.26%, 15–28 days: 75.47%) with no significant association (p=0.12). Maternal age also showed comparable CHD rates (75.00% vs 77.27%, p=0.88). Males (75.68%) and females (75.00%) had almost equal CHD occurrence (p=0.92). Mode of delivery showed similar distribution between SVD (74.19%) and C-section (75.63%) with no significant association (p=0.94). Birth weight ≤3.0 kg had slightly higher CHD frequency (84.62%) compared to ≥3.1 kg (73.39%), but this was not statistically significant (p=0.24).

Table 3: Association of effect modifiers with presence of congenital heart disease in IDMs (n = 150)

Effect Modifier	Category	CHD Present n (%)	CHD Absent n (%)	Total	χ^2	p-value
Infant age (days)	≤14	73 (75.26)	24 (24.74)	97	2.41	0.12
	15–28	40 (75.47)	13 (24.53)	53		
Maternal age (years)	20–35	96 (75.00)	32 (25.00)	128	0.02	0.88
	36–45	17 (77.27)	5 (22.73)	22		
Gender	Male	56 (75.68)	18 (24.32)	74	0.01	0.92
	Female	57 (75.00)	19 (25.00)	76		
Mode of delivery	SVD	23 (74.19)	8 (25.81)	31	0.01	0.94
	C-section	90 (75.63)	29 (24.37)	119		
Birth weight (kg)	≤3.0	22 (84.62)	4 (15.38)	26	1.35	0.24
	≥3.1	91 (73.39)	33 (26.61)	124		

Echocardiography was performed within 24 hours in 118 (78.67%) infants and within 24–72 hours in 32 (21.33%), shown in table 4. Overall, CHD was detected in 113 (75.33%) infants, while 37 (24.67%) had normal findings. Among affected infants, 77 (51.33%) were symptomatic at detection, whereas 36 (24.00%) were asymptomatic and identified only on echocardiography, highlighting its diagnostic value in early screening.

Table 4: Role of Echocardiography in Early Detection of Congenital Heart Disease in IDMs (n = 150)

Echocardiography Finding	Category	Frequency (n)	Percentage (%)
Timing of echocardiography	Within 24 hours of NICU admission	118	78.67
	24–72 hours of NICU admission	32	21.33
Detection of CHD	CHD detected	113	75.33
	No CHD detected	37	24.67
Clinical detection status	Symptomatic CHD detected on echo	77	51.33
	Asymptomatic CHD detected on echo	36	24.00
	No CHD (normal echo)	37	24.67

DISCUSSION

The present study revealed a high prevalence of CHD among IDMs (113, 75.33%) and only 37 IDMs (24.67%) did not have cardiac abnormalities on echocardiographic evaluation. The most frequent lesion was PDA in 42 (28.00%) cases, followed by septal hypertrophy in 19 (12.67%), VSD in 16 (10.67%), and atrial septal defect in 12 (8.00%). As in previous studies, it was also found that in IDMs, structural cardiac abnormalities were the most common lesions, with PDA and VSD being the most common, which is consistent with earlier findings of this study that there is strong association between maternal hyperglycemia and structural cardiac defects in organogenesis stages [7,13].

CHD spectrum was also seen in 15 (10.00%) cases, the transposition of great arteries (TGA) 6 (4.00%) and the tetralogy of Fallot (TOF) 3 (2.00%) cases showing a wide spectrum of complex cyanotic lesions with less prevalence. Similar results were noted in a study conducted in Lahore, in which PDA (26.87%), VSD (21.25%) and hypertrophic cardiomyopathy (17.50%) were found to be most common, whereas TGA and TOF were relatively rare (<11%) [7]. The similarities indicate that the dominant part of CHD in IDMs is acyanotic CHD in all populations.

In our study, the frequency of CHD was higher in infants ≤3.0 kg (84.62%) than in ≥3.1 kg (73.39%) infants, but the association was not statistically significant (p=0.24). This is in keeping with previous findings that that diabetic metabolism in pregnancy affects cardiac remodeling, including the development of septal hypertrophy in macrosomic fetuses. In a similar study, an international review suggested fetal hyperinsulinemia was associated with myocardial thickening and cardiac structural changes in diabetic pregnancy [14,15].

In terms of demographic and perinatal variables, in our study, CHD prevalence did not differ significantly among the groups of infant age ≤14 days vs 15–28 days (75.26% vs 75.47%, respectively; p>0.05), males vs females (75.68% vs 75.00%, respectively; p>0.05), or C-section vs SVD (75.63% vs 74.19%, respectively; p>0.05). The same results were found in another multicenter study that found no significant differences between the rate of CHD in IDMs and controls by either gender or delivery mode [16].

Our study demonstrated that the ability of echocardiography to provide a key role in the diagnostic process: of these 240CHDs, 113 (75.33%) were identified, with 36 (24.00%) being cases found only on the basis of screening. Importantly, 118 (78.67%) infants had echocardiograms within 24 hours, emphasizing the need for early imaging. Other studies have highlighted the importance of echocardiography in raising detection rates of occult CHDs, particularly in neonates without symptoms, thus enhancing early intervention opportunities and outcomes [17].

In general, the CHD distribution in our study was consistent with the high risk of IDMs for acyanotic CHD (PDA, VSD, septal hypertrophy) and the importance of echocardiography as a key diagnostic tool. This is in accordance with previous regional and international research demonstrating that poorly controlled glycemia during organogenesis is a significant risk factor for developing a neonatal structural congenital heart defect, especially with maternal diabetes [7].

Strength and Limitations of Study

The present study has certain advantages: the number of IDM included was limited to 150, and all had well-defined inclusion and exclusion criteria, and systematic echocardiographic evaluation of all suspected and asymptomatic neonates resulted in a high rate of diagnosis. The use of consecutive sampling lessened the likelihood of selection bias, and detailed sub-group analysis permitted the examination of the patterns of CHD in relation to various effect modifiers, including birth weight, gender, maternal age, and mode of delivery. The study, however, is limited by its single-center design, so it may not be generalizable to other groups. Another limitation of this relatively brief study period (six months), is the lack of long-term follow-up to assess outcomes or whether cardiac lesions detected during the study period progress or resolve. Furthermore, there are no biochemical indices of glycemic control in the mother to limit the assessment of direct association with the severity of CHD.

CONCLUSION

The study shows that there is a high prevalence of CHD in IDMs, and most of the abnormalities seen are PDA, septal hypertrophy and VSD. No statistically significant association was found between the occurrence of congenital heart disease and neonatal age, gender, maternal age, mode of delivery or birth weight (although there were more of these babies in the low birth weight group). Echocardiography was a very useful diagnostic tool in the detection of both symptomatic and asymptomatic IDMs admitted to NICU and its vital importance in early screening and timely and accurate detection of cardiac abnormalities.

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