DOI: https://doi.org/10.53350/pjmhs2023175172

ORIGINAL ARTICLE

Frequency of Cyanotic Heart Disease in Infants of Diabetic Mothers

MUHAMMAD IDREES[1], NAYAB SYED[2], ABID IMRAN[3], WAQAS IQBAL[4], ROMANA BIBI[5]
[1,2,3]*Specialist Registrar Department of Pediatrics, Hayatabad Medical Complex, Peshawar*
[4]*Medical Officer Darra Adamkhel Welfare Hospital, KPK, Pakistan*
[5]*Postgraduate Resident Gynae/Obs Khyber Teaching Hospital Peshawar*
Correspondence to Dr. Abid Imran, Email: drabidimran86@yahoo.com

ABSTRACT

Aim: To determine the frequency of cyanotic heart disease in infants born to diabetic mothers referred to Tertiary Care Hospital.
Materials: This Cross-Sectional Study was conducted in the Pediatrics Department of Hayatabad Medical Complex, Peshawar from July 2021 to July 2022. In this study, a total of 262 patients were to determine the frequency of cyanotic heart disease in infants born to diabetic mothers referred to the Pediatrics Department of Hayatabad Medical Complex, Peshawar. The sampling technique was non-probability consecutive sampling.
Results: The age of the participants among 262 patients was analyzed as n= 1-15 Days was 170(64.9%) 16-28 Days was 92(35.1%). The mean age was 9±1.87 days. The distribution of gender among 262 patients was analyzed as n= Male was 142(54.2%) and Female was 120(45.8%).The distribution of weight among 262 patients was analyzed as n= less than or Equal to 4.5 kg was 126(48.1%) and More than 4.5 kg was 136(51.9%). Mean weight 5.1±1.87kg. Distribution of Duration of diabetes in mothers (years) among 262 patients was analyzed as n= 1-5 Years was 135(51.5%) and More than 6 Years was 127(48.5%). Mean duration was7.1±1.12 years. The distribution of Cyanotic Heart Disease among 262 patients was analyzed as n= Yes was 48(18.3%) and No was 214(81.7%).
Practical implication: To determine the frequency of cyanotic heart diseases in children born of a diabetic mother, its prompt diagnosis and management to reduce neonatal morbidity and mortality.
Conclusion: In this high-risk population useful assessment and early CHD diagnosis are strongly suggested, and echocardiography is advised as soon as feasible for all newborns of diabetes mothers. Prenatal CHD screening program for neonates of diabetes moms are required in our setup. Therefore, additional confirmation is anticipated in a study of a larger diabetic population.
Keywords: Gestational diabetes mellitus, Congenital heart diseases, pre-gestational diabetes mellitus, Diabetic mothers

INTRODUCTION

Chromosomal abnormalities (trisomies 21,18,13), microdeletions of chromosome 22q11.2, untreated maternal diabetes, maternal consumption of retinoic acid, phenylketonuria, and Alagille syndrome with JAG1/NOTCH2 mutations have all been linked to the development of cyanotic heart disease.[1]Mutations in the transcription factor NKX2.5, polymorphisms of the enzyme methylenetetrahydrofolatereductase, and mutations in the genes TBX1 and ZFPM2 are some further genetic anomalies associated with a tendency to cyanotic cardiac disease[2,3].

Patients with cyanotic heart illness frequently have ventricular septal abnormalities that are perimembranous and can extend into the muscular septum[4]. Numerous factors, such as the pulmonary valve, which is typically bicuspid and stenotic, the hypoplastic pulmonary valve annulus, the deviation of the infundibular septum, which results in a subvalvular obstruction, and the hypertrophy of the muscular bands in this area, can all contribute to the right ventricular outflow obstruction[5]. Both ventricles provide blood to the overriding aorta, which often differs in degree. A right-to-left shunt across the ventricular septal defect, resulting in marked desaturation, is the physiological process underlying the hyper cyanotic episodes or "Tet spells" in cyanotic heart disease[6].

Despite improvements in our knowledge of the genetic causes of congenital heart disease (CHD) over the past ten years[7], since many years ago, it has been known that maternal diabetes mellitus developing in the early stages of pregnancy increases the chance of developing certain diseases[8]. Recent population-based observations have shown links between various maternal cardiometabolic diseases, such as obesity, and the risk of CHD in the childrens[9]. It is complicated to determine which of the numerous phenotypic overlaps between diabetes mellitus, obesity, and cardiometabolic risk is responsible for the danger to the foetus when present in the mother during the early stages of pregnancy[10].

Received on 07-12-2022
Accepted on 17-04-2023

According to a study by Shamaoon M et al., 2.8% of children delivered to diabetes moms had cyanotic cardiac disease[11]. In a another study by Shankar P. et al., it was , the children delivered to diabetes moms had cyanotic heart disease 28.6% of the time[12].

The real incidence and prevalence of cyanotic heart disease in Pakistan remain unclear since there is insufficient access to medical treatment and funding for a comprehensive population study.In the country, there is no specific facility for the diagnosis of cyanotic heart disease. In order to ascertain the prevalence of cyanotic heart disease in children delivered to diabetes mothers who were referred to the pediatrics department of the Hayatabad Medical Complex, Peshawar. It would be helpful to minimize potential cyanotic heart disease consequences and enhance quality of life by early detection/diagnosis of the condition in newborns of diabetes mothers.

MATERIAL AND METHODS

This Cross-Sectional Study was conducted in the Pediatrics Department of Hayatabad Medical Complex, Peshawar from July 2021 to July 2022 after permission from Institutional Ethical Committee. Sample size of 262 patients is calculated by using WHO sample size formula using an expected frequency of cyanotic heart disease by 2.8% in infants born to diabetic mothers[11]. Margin of error= 2% and Confidence level = 95%, with Non-probability consecutive sampling technique. Patients both males and females with age 1-28 days, admitted to NICU with mother having diabetic historieswere included in this study. While neonates born at < 25 weeks of GA on LMP, family history of Down syndrome and parents refused for consent were excluded.
Data collection procedure: After receiving approval from the ethics committee, children meeting the inclusion criteria from the pediatrics department of the Hayatabad Medical Complex in Peshawar will be enrolled in the study. Each parent gave their informed permission after being assured of the study's confidentiality and the absence of any harm to the patient.
There will be two-dimensional echocardiography with Doppler vascular analysis. The same cardiologist with three years of post-fellowship experience carried out and assessed each study to assure validity. According to the operational definition, cyanotic

heart disease will be identified. A specifically created proforma will record the presence of cyanotic heart disease.

The SPSS version 22 statistical analysis program was used to enter and analyze the data. For quantitative characteristics like age, the length of moms' diabetes, and weight, the mean and standard deviation will be reported..In order to account for qualitative factors like gender and a cyanotic heart condition, frequency and percentage were computed. The risk of cyanotic heart disease will be stratified according to age, gender, the length of a mother's diabetes, and weight. A post-stratification chi-square test will be used, and statistical significance will be determined by p=0.05.

RESULTS

Age of the participants among 262 patients were analyzed as n= 1-15 Days was 170(64.9%) 16-28 Days was 92(35.1%) Mean age was 9±1.87 days. Distribution of gender among 262 patients were analyzed as n= Male was 142(54.2%) and Female was 120(45.8%). Distribution of weight among 262 patients were analyzed as n= less than or Equal to 4.5 kg was 126(48.1%) and more than 4.5kg was 136(51.9%). Mean weight 5.1±1.87kg. Distribution of Duration of diabetes in mothers (years) among 262 patients were analyzed as n= 1-5 Years was 135(51.5%) and More than 6 Years was 127(48.5%). Mean duration was7.1±1.12 years. Distribution of Cyanotic Heart Disease among 262 patients were analyzed as n= Yes was 48(18.3%) and No was 214(81.7%) (Table 2).

Table-1: Demographics of patients

	Frequency	Percentages
Age of the participants		
1-15 Days	170	64.9
16-28 Days	92	35.1
Gender wise Distribution		
Male	142	54.2
Female	120	45.8
Weight		
less than or Equal to 4.5 kg	126	48.1
More than 4.5 kg	136	51.9
Duration of diabetes in mothers (years)		
1-5 Years	135	51.5
More than 6 Years	127	48.5

Table-2: Stratification of Cyanotic Heart Disease with gender

Male	Female	Total
31(84.6%)	17(35.4%)	48(100%)
111(51.9%)	103(48.1%)	214(100%)
Total		
142(54.2%)	120(45.8%)	262(100%)

P value 0.110

Table 3: Stratification of Cyanotic Heart Disease with Duration of Diabetes in Mother

Duration of diabetes in mothers(years)		Total
1-5Years	**More than 6 Years**	
29(60.4%)	19(39.6%)	48(100%)
106(49.5%)	108(50.5%)	214(100%)
Total		
135(51.5%)	127(48.5%)	262(100%)

P value 0.173

DISCUSSION

If diabetes mellitus is present in a pregnant woman, it poses a serious risk to the fetus. Up to this point, reports have primarily highlighted the population of mothers with type 1 diabetes[13-15]. There is mounting evidence that type 2 diabetes-suffering women's fetuses may be predisposed to a comparable condition that causes issues with a variety of the fetus and placenta's organ systems[16-19]. Congenital cardiac abnormalities were only found in 2(4.7%) of the 42 children of diabetes mothers in local research conducted at this facility[20]. Results of a study revealed that, after PDA and hypertrophic cardiomyopathy (HCMP) patients were excluded, the total incidence of congenital cardiac disorders was 9.3%[21].

According to the findings of a local study carried out in Lahore, 1530 full-term neonates were registered, of which 84(6%) were children of diabetes mothers (IDMs[22]. In contrast, we discovered that a significant portion of IDMs (52.5%) had diverse congenital cardiac disorders. The fact that we had a relatively limited sample size for this hospital-based investigation may be the cause of the increased prevalence of congenital cardiac disease in the IDM group of our study.

The second explanation could be because the majority of these infants were born in this hospital, and the gynecologists and obstetricians immediately sent them to the NICU for the early identification and diagnosis of CHD. A local study conducted at this facility found that 13(31%) and 29(69%) of the newborn babies of diabetes moms were females[20]. 9614 children were admitted in total to pediatric wards throughout the research period, according to another local study. 96 of them had congenital cardiac disease, according to documented cases.. 64 male and 32 female patients made up the 2:1 ratio[23]. Similar findings were also obtained in our study, which had a male-to-female ratio of 1.97 with a majority of 66.30% men and 33.7% women. In our study, which was primarily male, and in several other studies conducted throughout the nation, the findings were likewise consistent[24-26].

Burki found a similar prevalence in both sexes in one Hazara survey[27]. According to a study, babies of pre-pregnant and gestational diabetes moms had congenital heart disease incidence rates of 49(65%) and 36(35%) respectively[21]. Another study revealed that 63(75%) mothers had gestational diabetes, whereas 21 (25%) of the diabetic moms had developed diabetes mellitus[22].The findings of our study revealed that pre-gestational diabetes affected 45.5% of mothers of newborns and that it affected 54.5% of moms who had diabetes during pregnancy. Studies' outcomes may vary depending on the sample sizes used, and whether moms receive prenatal care often or seldom may have an impact on their diabetes status. Fetal CHD is known to be more likely in women with maternal diabetes mellitus (MDM), with an estimated risk increase of up to 8.5% in live births. MDM has been linked to the majority of cardiac structural abnormalities, from minor septal defects to duct-dependent heart disease[28,29].

Numerous studies conducted at the national and international levels report similar frequencies in a more-or-less consistent manner. The diverse sample size choices and lengths of research periods are to blame for variations in the frequency of distinct CHD in all studies. Due to the fact that we have a relatively short research period while only a small number of studies have investigated their patients for up to five years. A 9-month observational prospective research examined infants of moms with GDM who were recruited. 65 infants delivered to 82 women who had poor glucose metabolism participated in the research. 11(16.9%) patients had patent ductus arteriosus (PDA), 4(6.2%) had moderate pulmonary stenosis and 23(33.8%) had hypertrophy of the ventricular septum[30].

The most prevalent echocardiographic findings in one study included patent ductusarteriosus (PDA) in 54.7% of cases, hypertrophic cardiomyopathy (HCMP) in 24%, ventricular septal defect (VSD) in 4%, atrial septal defect (ASD) in 2.7%, transposition of the great arteries (TGA) in 1.3%, and coarctation of the aorta (COA) in 1.3% of cases.[21]According to the findings of a local research carried out in Lahore, 84(6%) of the 1530 full-term neonates who were recorded in the study were children of diabetes mothers (IDMs). 11(13%) of the IDMs had congenital abnormalities, with congenital heart disease being the most common.

According to a Saudi Arabian study, patent ductus arteriosus (PDA), patent foramen ovale (PFO), atrial septal defect (ASD), small muscular ventricular septal defect, mitral valve prolapse, and pulmonary stenosis were the most frequent echocardiographic findings in infants of diabetics..According to a recent study, asymmetrical septal hypertrophy, patent foramen ovale (PFO), and

patent ductus arteriosus (PDA) were the three most prevalent echocardiographic abnormalities in IDMs[32]. Early CHD discovery is crucial for good therapy since it helps to prevent problems. Examining babies at maternity units, postpartum clinics, special baby care units, immunisationcentres, primary Health care units, and at school entry can do this[24].

CONCLUSION

In this high-risk population useful assessment and early CHD diagnosis are strongly suggested, and echocardiography is advised as soon as feasible for all newborns of diabetes mothers. Prenatal CHD screening program for neonates of diabetes moms are required in our setup.Therefore, additional confirmation is anticipated in a study of a larger diabetic population.

Conflict of interest: Nil

REFERENCES

1. Khan SM, Drury NE, Stickley J, Barron DJ, Brawn WJ, Jones TJ, et al. Tetralogy of fallot: morphological variations and implications for surgical repair. Eur J Cardiothorac Surg. 2019;56(1):101-9. doi: 10.1093/ejcts/ezy474.
2. Apostolopoulou SC, Manginas A, Kelekis NL, Noutsias M. Cardiovascular imaging approach in pre and postoperative tetralogy of Fallot. BMC Cardiovasc Disord. 2019;19(1):7.doi: 10.1186/s12872-018-0996-9.
3. Wise-Faberowski L, Asija R, McElhinney DB. Tetralogy of fallot: everything you wanted to know but were afraid to ask. Paediatr Anaesth. 2019;29(5):475-82. doi: 10.1111/pan.13569.
4. Ho AB, Bharucha T, Jones E, Thuraisingham J, Kaarne M, Viola N. Primary surgical repair of tetralogy of fallot at under three months of age. Asian CardiovascThorac Ann. 2018;26(7):529-34. doi: 10.1177/0218492318803037.
5. Mcleod G, Shum K, Gupta T, Chakravorty S, Kachur S, Bienvenu L, et al. Echocardiography in congenital heart disease. Prog Cardiovasc Dis. 2018;61(5-6):468-75. doi: 10.1016/j.pcad.2018.11.004.
6. Rao PS. Management of congenital heart disease: state of the art-part ii-cyanotic heart defects. Children. 2019;6(4):54. doi: 10.3390/children6040054.
7. Blue GM, Kirk EP, Giannoulatou E, Sholler GF, Dunwoodie SL, Harvey RP, et al. Advances in the genetics of congenital heart disease: a clinician's guide. J Am CollCardiol. 2017;69:859–70. doi: 10.1016/j.jacc.2016.11.060.
8. Mitanchez D, Yzydorczyk C, Simeoni U. What neonatal complications should the pediatrician be aware of in case of maternal gestational diabetes?.World J Diabetes. 2015;6(5):734-43. doi: 10.4239/wjd.v6.i5.734.
9. Persson M, Razaz N, EdstedtBonamy AK, Villamor E, Cnattingius S. Maternal overweight and obesity and risk of congenital heart defects. J Am CollCardiol. 2019;73:44–53. doi: 10.1016/j.jacc.2018.10.050.
10. Helle E, Priest JR. Maternal obesity and diabetes mellitus as risk factors for congenital heart disease in the offspring. J Am Heart Assoc. 2020;9(8):e011541. doi: 10.1161/JAHA.119.011541.
11. Shamaoon M, Zunaira T, 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):950-6. DOI: https://doi.org/10.29309/TPMJ/2020.27.05.3924
12. Shankar P, Marol JS, Lysander SD, Manohar A. Cardiovascular malformations in infants of diabetic mothers: a retrospective study. Int J ContempPediatr. 2019;6:1998-2002.
13. Weber HS, Gleason MM, Myers JL, et al. The Fontan operation in infants less than 2 years of age. J Am CollCardiol. 1992 Mar 15. 19(4):828-33. https://doi.org/10.1016/0735-1097(92)90526-S
14. Smythe JF, Copel JA, Kleinman CS. Outcome of prenatally detected cardiac malformations. Am J Cardiol. 1992 Jun 1. 69(17):1471-4. doi: 10.1016/0002-9149(92)90903-c.
15. Fogel MA. Is routine cardiac catheterization necessary in the management of patients with single ventricles across staged Fontan reconstruction? No!.PediatrCardiol. 2005 Mar-Apr. 26(2):154- 8. doi: 10.1007/s00246-004-0960-6.
16. Hirono K, Yoshimura N, Taguchi M, et al. Bosentan induces clinical and hemodynamic improvement in candidates for rightsided heart bypass surgery. J ThoracCardiovasc Surg. 2010 Aug. 140(2):346-51. doi: 10.1016/j.jtcvs.2010.03.023.
17. Hirono K, Yoshimura N, Taguchi M, et al. Bosentan induces clinical and hemodynamic improvement in candidates for rightsided heart bypass surgery. J ThoracCardiovasc Surg. 2010 Aug. 140(2):346-51. doi: 10.1016/j.jtcvs.2010.03.023.
18. Puga FJ, Chiavarelli M, Hagler DJ. Modifications of the Fontan operation applicable to patients with left atrioventricularvalve atresia or single atrioventricular valve. Circulation. 1987 Sep. 76(3 Pt 2):III53-60.
19. Jonas RA, Castaneda AR. Modified Fontan procedure: atrial baffle and systemic venous to pulmonary arteryanastomotic techniques. J Card Surg. 1988 Jun. 3(2):91-6. doi: 10.1111/j.1540-8191.1988.tb00228.x.
20. deLeval MR, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations. Experimental studies and early clinical experience. J Thorac Cardiovasc Surg. 1988 Nov. 96(5):682- 95.
21. Marcelletti C, Corno A, Giannico S, Marino B. Inferior vena cavapulmonary artery extracardiac conduit. A new form of rightheart bypass. J ThoracCardiovasc Surg. 1990 Aug. 100(2):228- 32.
22. Laschinger JC, Ringel RE, Brenner JI, McLaughlin JS. Extracardiac total cavopulmonary connection. Ann Thorac Surg. 1992 Aug. 54(2):371-3. doi: 10.1016/0003-4975(92)91407-z.
23. Bridges ND, Mayer JE, Lock JE, et al. Effect of baffle fenestration on outcome of the modified Fontan operation. Circulation. 1992 Dec. 86(6):1762-9. doi: 10.1161/01.cir.86.6.1762.
24. Lemler MS, Scott WA, Leonard SR, et al. Fenestration improves clinical outcome of the fontan procedure: a prospective, randomized study. Circulation. 2002 Jan 15. 105(2):207-12. doi: 10.1161/hc0202.102237.
25. Monagle P, Cochrane A, Roberts R, Manlhiot et al. A multicenter, randomized trial comparing heparin/warfarin and acetylsalicylic Acid as primary thromboprophylaxis for 2 years after the fontan procedure in children. J Am Coll Cardiol. 2011 Aug 2. 58(6):645-51. doi: 10.1016/j.jacc.2011.01.061.
26. Potter BJ, Leong-Sit P, Fernandes SM, Feifer A, Mayer JE Jr, Triedman JK, et al. Effect of Aspirin and warfarin therapy on thromboembolic events in patients with univentricular hearts and Fontan palliation. Int J Cardiol. 2013 Jul 17. doi: 10.1016/j.ijcard.2013.06.058.
27. Mertens L, Hagler DJ, Sauer U, et al. Protein-losing enteropathy after the Fontan operation: an international multicenter study. PLE study group. J ThoracCardiovasc Surg. 1998 May. 115(5):1063- 73. doi: 10.1016/s0022-5223(98)70406-4.
28. Minamisawa S, Nakazawa M, Momma K, et al. Effect of aerobic training on exercise performance in patients after the Fontan operation. Am J Cardiol. 2001 Sep 15. 88(6):695-8. doi: 10.1016/s0002-9149(01)01822-7.
29. Coon PD, Rychik J, Novello RT, et al. Thrombus formation after the Fontan operation. Ann Thorac Surg. 2001 Jun. 71(6):1990- 4. doi: 10.1016/s0003-4975(01)02472-9.
30. Ravn HB, Hjortdal VE, Stenbog EV, et al. Increased platelet reactivity and significant changes in coagulation markers after cavopulmonary connection. Heart. 2001 Jan. 85(1):61-5. doi: 10.1136/heart.85.1.61.
31. Cohen MI, Bush DM, Ferry RJ, et al. Somatic growth failure after the Fontan operation. Cardiol Young. 2000 Sep. 10(5):447- 57. doi: 10.1017/s1047951100008118.
32. Ono M, Boethig D, Goerler H, Lange M, Westhoff-Bleck M, Breymann T. Somatic development long after the Fontan operation: factors influencing catch-up growth. J ThoracCardiovasc Surg. 2007 Nov. 134(5):1199-206. doi: 10.1016/j.jtcvs.2007.08.002.