



Original Article

<http://wjpn.ssu.ac.ir>

Prevalence of Congenital Heart Diseases in Neonates of Diabetic Mothers: A Cross Sectional Study in Yazd

Mohamad Hosein Lookzadeh¹, Mohammad Reza Alipour², Abbas Vakili-Zarch³, Sedigheh Ekraminasab^{1,4*}¹ Mother and Newborn Health Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran² Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran³ Department of Surgery, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran⁴ Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 01 May 2022

Revised: 09 June 2022

Accepted: 29 June 2022

ARTICLE INFO

Corresponding author:

Sedigheh Ekraminasab

Email:

s.ekraminasab@gmail.com

Keywords:Infants,
Congenital,
Heart Defects,
Maternal,
Diabetes Mellitus,
Echocardiography

ABSTRACT

Background: Maternal hyperglycemia is a critical risk factor for congenital heart diseases (CHD). Despite advancements in the medical management of diabetic mothers, the CHD in their infants are still more recurring compared to infants of the general population. The primary purpose of this investigation was to explore the prevalence of CHD in infants of diabetic mothers (IDMs). The study was also aimed at investigating possible associations between the types of maternal diabetes with the incidence of CHD in IDMs especially the status of diabetic control.

Methods: This cross-sectional study was performed between October 2016 and September 2017, in a Heart Center in Yazd. The cases were comprised of 150 neonates of mothers with diabetes. We determined CHD via fetal echocardiography during the first day of childbirth and estimated the prevalence of CHD in IDMs and its association to control status of diabetes in mothers.

Results: The prevalence of CHD in IDMs was 12.7%. The results showed that there was a significant relationship between maternal uncontrolled diabetes and a high incidence of CHD in IDMs ($P \leq 0.0001$), but there was no association between the type of diabetes and the incidence of HCM.

Conclusion: We concluded that controlling maternal diabetes has the greatest effect on the prevention of CHD in neonates. The prevalence of CHD in IDMs was 12.7% which is high that may be due to poor control of diabetes in pregnant women in Iran. Also, neonates of diabetic mothers need more cardiac evaluation tests and follow-ups. Therefore, more studies on the effects of maternal diabetes-induced CHD in neonates are needed.

Introduction

Congenital heart disease (CHD) is the most prevalent birth defect in the worldwide.¹ CHD is the most common reason of death from congenital disabilities in neonates and is usually related to fetal loss.² It results in 1-1.5% of global mortality among pediatric under 5 years of age.³ The incidence of CHD is approximately 6 to 8 cases per 1000 live births globally.⁴ CHD affects about 1% of (about 40,000) births per year in the USA.⁵ Although many pediatric with CHD need no surgical intervention, approximately 1 in 4 children with CHD need cardiac surgery.¹ The exact cause of most CHD is unknown, but some risk factors have been identified. Studies have demonstrated that complex combinations of environmental teratogens, genetic and maternal factors play a role in susceptibility to the CHD.⁶ Maternal diabetes mellitus (DM) is one of these factors that have a teratogenic effect on the fetal heart. Maternal DM during pregnancy has detrimental health impacts on both the mother and fetus, such as cardiac malformations, cesarean section (CS), asphyxia and etc.⁷ In pregnant women, the excess amounts of blood glucose are transferred to the fetus. This causes the fetus's body to secrete increased amounts of insulin, which causes several disorders in the neonates. Diabetes, with a prevalence rate of 10-30% in pregnancy, is one of the main causes of intrauterine growth deficiencies and congenital anomalies. Studies have shown that the risk of fetal anomalies in diabetic mothers is 4-5 times higher than non-diabetic mothers.⁸ The incidence of cardiac anomalies is 3-6% more prevalent in infants of diabetic mothers (IDMs). Also CHD in these infants is five times higher than in normal pregnancies and most of the time it contains complex forms.^{9,10} As established by the statistics, the incidence rate of CHD in the normal population is 0.39-0.39%, while this rate is 2.8-21% in IDMs.⁸ Studies propose that IDMs undergo a fetal programming result due to the

hyperglycaemic intrauterine environment which increases their risk of cardiovascular morbidity in adult life.¹¹ In other words embryogenesis in a condition with high glucose concentration harms cardiac morphogenesis.⁹ Maternal DM greatly influences the fetal heart and fetal -placental circulation in both function and structure. A current study demonstrated that the severity of hyperglycemia in the first trimester is related to a higher incidence of CHD. Likewise, even a mild height of glucose levels has been documented to induce CHD and deep teratogenic effect during the first week of pregnancies.¹²

Antenatal evaluation of the cardiac structures and function can be assessed with fetal echocardiography and electrocardiography.¹³ Also more proper glycemic control of diabetic mothers is related to a lower happening of fetal heart disease but not necessarily with the lower expansion of fetal myocardial hypertrophy.⁹

There is limited data on the prevalence of CHD in neonates of diabetic mothers in Yazd. For this purpose, we assessed CHD prevalence in IDMs in a Heart Center in Yazd. We examined associations between types of maternal diabetes and the prevalence of CHD in IDMs. We also want to investigate the possible association of neonatal CHD with controlled and uncontrolled maternal diabetes.

Materials and Methods

This cross-sectional study was performed between October 2016, and September 2017. The 150 neonates of diabetic mothers were enrolled in this investigation. After approval from the Research Ethics Committee of the Shahid Sadoughi University, all patients were admitted to the study voluntarily and received written consent. Data has been dragged from patients' files and documented. Ultimately, the information related has been operated in keeping with statistical analysis. The research included singleton fetuses of pregnant women identified with diabetes, without malformations and other disorders that could

interfere with fetal growth. The identification of diabetes was established on the standards provided by the American Diabetes Association (ADA), that is, blood glucose (sugar) level. To assess hereditary heart problems in neonates, myocardial thickness, left ventricular myocardial performance index (LVMPI), shortening fraction and right ventricular myocardial performance index (RVMPI), and tricuspid flow and mitral E/A ratio were assessed in echocardiographic tests with Doppler.

Statistical analysis: All variables were descriptively investigated, with quantitative variables represented as mean and standard deviations. Data were statistically analyzed utilizing the Statistical software (SPSS version 20). The analysis and frequency were calculated using the T-student and chi-square tests with the 95% confidence interval (95% CI).

Results

In this cross-sectional study, 150 infants of diabetic mothers who had been referred to the Yazd Heart Clinic were studied and followed up by a neonatologist and cardiologist. All the neonates were full-term and singleton without other syndrome and genetic disorders. The following results were obtained. We categorized diabetic mothers by type of diabetes, 43 mothers had type I diabetes and 107 mothers had type II diabetes (Table 1). Examination of maternal blood sugar and HBA1C in the first trimester of pregnancy showed that diabetes was controlled in 126 mothers (84%) and not controlled in 24 mothers (16%) (Table1). Examination of neonatal echocardiography among 150 neonates that were born from diabetic mothers, 19 neonates had a kind of CHD. So the overall prevalence of CHD in neonates of

diabetic mothers was 12.7%.

In our study, 71.3% were found to have Type II diabetes and we did not find a significant relationship between maternal diabetes types and the rate of CHD in their neonates. Out of the 19 babies who showed CHD cardiac abnormality, 18 babies were born to mothers with uncontrolled diabetes and 1 baby was born to mothers with controlled diabetes, so there is a significant relationship between the types of controlled diabetes with the incidence of CHD in these neonates.

Discussion

The prevalence of pregestational and gestational diabetes has been expanding globally.¹⁴ In pregnancies involved by diabetes, the diabetic intrauterine environment could cause placental dysfunction and hormonal alterations, leading to CHD, obesity, and diabetes in neonates.¹⁵

Maternal DM negatively influences fetal condition by increasing the risk of perinatal morbidity and mortality. Additional CHD is the most significant single reason for perinatal mortality amongst the IDMs¹⁶ Because the incidence of diabetes in Asian women is higher than in European and American women and is still increasing, so the incidence of CHD is higher in Asian countries than in other parts of the world.⁷

There is a diverse range of prevalence of CHD reported in IDMs. Investigations performed in Iran have estimated the prevalence of CHD in the range of 9.3 to 18.7 per 1000 live births.^{9,17,18,19} Although most studies have divided maternal diabetes into gestational and pregestational diabetes, we just focused on maternal diabetes types I or II and diabetes control and then evaluate the incidence of CHD in that groups.

Table 1. Prevalence of CHD in Neonates of Diabetic Mothers in Subtype

Variable		Number (%)	Number (%) of CHD	P
Type of Diabetes (n = 150)	Type I	43 (28.7)	7 (16.3)	< 0.277
	Type II	107 (71.3)	12 (11.2)	
Controlled Diabetes (n = 150)	No	24 (16)	18 (75)	≤ 0.0001
	Yes	126 (84)	1 (0.8)	

In our study the prevalence of CHD in IDMs was 12.7% which is high that may be due to poor control of diabetes in pregnant women in Iran. Several studies assessed the prevalence of CHD in IDMs in the Iranian population. Most of them, similar to us, reported a high prevalence of CHD in IDMs. Bahjati et al., in 2011, evaluated CHD in 75 IDMs. In their study, the incidence of CHD was relatively high with about 93 per thousand (9.3%) of infants born to mothers with diabetes mellitus. They hypothesized that the high incidence of CHD in their study could be mainly due to the diagnosis of small lesions such as ASD Small, which close after a few months. It may also be due to poor control of maternal diabetes during gestation, genetics or other environmental factors.²⁰ Roodpeyma et al., in 2013 evaluated Cardiovascular Complications in IDMs. They studied a total of 32 IDMs. Their results showed CHD was 18.7% of neonates that was a high prevalence of CHD in IDMs in their pediatric cardiology clinic. In their results neither the types of maternal diabetes nor the somatic findings of neonates were related to the happening of cardiovascular abnormalities.⁹ Arjmandnia et al., in 2019 assessed the prevalence of CHD in 200 neonates of diabetic mothers who were referred to teaching hospitals in Qom, Iran. Their study showed that echocardiographic results were abnormal in 49% of neonates of diabetic mothers. Based on the results, it was concluded that 9 out of each 10 diabetic neonates have CHD, that PFO being the most common one of them.⁸ In 2021 in a retrospective cohort study in Saudi Arabia, Alyousif et al., evaluated incidence of CHD in infants of diabetic mothers. They assessed 1838 diabetic mothers; and showed incidence of CHD among IDMs in their cohort study was 11.82%. Also they indicated the incidence of CHD was higher among mothers who had type 1 diabetes followed by type 2 diabetes.²¹ Arul et al., in 2019 assessed range of cardiac complications in neonates born to diabetic mother. In their study, 100 IDMs

were subjected to ECG; of this, 28 (28%) neonates had cardiac abnormality. A similar study done on cardiovascular abnormalities in IDM by Meyer et al., demonstrated a lower incidence of 3.2 to 6.9 and a study by Tabib et al., showed an incidence of 8.8%.¹⁰ Abu-Sulaiman et al., evaluated CHD in 100 Infants of Diabetic Mothers. Overall incidence of CHD was 15% after excluding PDA and HCMP and the maternal diabetic control was poor.²²

Generally according to our results and other studies the incidence of CHD in IDMs still high, especially in Asian country that is an indication of poor control of diabetes during pregnancy. However the high frequency of CHD in our IDMs group may be due to the influence of the environmental factors as well as to the high maternal blood glucose level. Our results showed that CHD could not be related to the type of maternal diabetes and no difference between type I and type II diabetes. But some belief that pregnancies complicated by type II diabetes and gestational diabetes must be referred for detailed fetal cardiac evaluation and type I diabetes is not so important.¹⁶ In this study only the control of maternal diabetes has a significant effect on the prevention of CHD in neonates. It requires more studies to differentiate gestational diabetes from diabetic mothers and to estimate the prevalence of CHD in gestational and pregestational diabetic mothers. Also a multicenter study with large sample size is needed to determine the exact prevalence of CHD.

Conclusion

In conclusion, our study demonstrated there is still a high frequency of CHD in the IDMs group. This study showed that CHD is not be related to the type of maternal diabetes but there is a significant relation between control of maternal diabetes and prevalence of CHD. The influence of glycemic control on cardiac function in IDMs should be evaluated using both conventional echocardiography and tissue Doppler imaging. Therefore, it is

necessary to effective control of maternal diabetes and determines the screening method in these neonates.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The authors thank the editors and the anonymous reviewers for insightful suggestions on this study.

How to Cite: Lookzadeh MH, Alipour MR, Vakili-Zarch A, Ekraminasab S. Prevalence of Congenital Heart Diseases in Neonates of Diabetic Mothers: A Cross Sectional Study in Yazd. *World J Peri & Neonatol* 2022; 5(1): 24-9. DOI: 10.18502/wjpn.v5i1.10125

References

- Greenberg JH, McArthur E, Thiessen-Philbrook H, Zappitelli M, Wald R, Kaushal S, et al. Long-term Risk of Hypertension after Surgical Repair of Congenital Heart Disease in Children. *JAMA Netw Open* 2021;4(4): 1-13.
- Blue GM, Kirk EP, Sholler GF, Harvey RP, Winlaw DS. Congenital heart disease: Current knowledge about causes and inheritance. *Med J Aust* 2012; 197(3):155-9.
- Chen L, Yang T, Chen L, Wang L, Wang T, Zhao L, et al. Risk of congenital heart defects in offspring exposed to maternal diabetes mellitus: an updated systematic review and meta-analysis. *Arch Gynecol Obstet.* 2019; 300(6): 1491-506.
- Peyvandi S, Baer RJ, Chambers CD, Norton ME, Rajagopal S, Ryckman KK, et al. Environmental and socioeconomic factors influence the live-born incidence of congenital heart disease: A population-based study in California. *J Am Heart Assoc* 2020; 9(8): 1-11.
- Krasuski RA, Bashore TM. Congenital Heart Disease Epidemiology in the United States: Blindly Feeling for the Charging Elephant. *Circulation* 2016; 134(2): 110-3.
- Wong P, Denburg A, Dave M, Levin L, Morinis JO, Suleman S, Wong J, Ford-Jones E, Moore AM. Early life environment and social determinants of cardiac health in children with congenital heart disease. *Paediatr Child Health* 2018; 23(2): 92-95.
- Stuart, A. Maternal diabetes during pregnancy –obstetrical considerations and long term effects. [Thesis]. Department of Obstetrics and Gynecology, Lund University. 2012.
- Arjmandnia MH, Yousefi M, Rezvan S, Vahedian M, Noori E, Mohammadi A, et al. Evaluation of Congenital Heart Diseases in Neonates with Diabetic Mothers Who Referred to Teaching Hospitals in Qom, Iran. *J Vessel Circ* 2020; 1(1): 33-6.
- Roodpeyma S, Rafieyian S, Khosravi N, Hashemi A. Cardiovascular complications in infants of diabetic mothers: An observational study in a pediatric cardiology clinic in Tehran. *J Compr Pediatr* 2013; 4(2): 119-23.
- Arul AS, Babu Kandha Kumar AS, Kiruthiga K, Priya MK, Neveythaa SA. Spectrum of cardiovascular abnormalities in infants born to diabetic mother in a tertiary care center. *Indian J Cardiovasc Dis Women WINCARS* 2019; 4(3): 124-8.
- Russell NE, Higgins MF, Kinsley BF, Foley ME, McAuliffe FM. Heart rate variability in neonates of type 1 diabetic pregnancy. *Early Hum Dev.* 2016; 92: 51-5.
- Chou FS, Chakradhar R, Ghimire LV. Socioeconomic and racial disparities in the prevalence of congenital heart disease in infants of diabetic mothers. *J Matern Neonatal Med* 2021; 34(24): 4167-70.
- Al-Biltagi M, El razaky O, El Amrousy D. Cardiac changes in infants of diabetic mothers. *World J Diabetes* 2021; 12(8): 1233-47.
- Sobeih AA, Sakr MMA, Abolmaaty RK. Assessment of cardiac diastolic function in infants of diabetic mothers using tissue Doppler echocardiography. *Egypt Pediatr Assoc Gaz* 2020; 68(1).
- Yu Y, Arah OA, Liew Z, Cnattingius S, Olsen J, Sørensen HT, et al. Maternal diabetes during pregnancy and early onset of cardiovascular disease in offspring: Population based cohort study with 40 years of follow-up. *BMJ* 2019; 367(Cvd): 1-4.
- Petropoulos AC, Xudiyeva A, Ismaylova M. Congenital heart disease and maternal diabetes mellitus. *EJCS* 2018; 1(3): 32-9.
- Atary SK, Mirshahi A, Amouzeshi A, Ramazani AA, Khomartash ZS, Bahman B, et al. Epidemiologic Study of Congenital Heart Diseases and Its Related Factors in Children

- Referred to the Pediatric Cardiac Clinic of Birjand University of Medical Sciences, Iran. *Int J Pediatr* 2019; 7(12): 10455-63.
18. Nazari P, Davoodi M, Faramarzi M, Bahadoram M, Dorestan N. Prevalence of Congenital Heart Disease: A Single Center Experience in Southwestern of Iran. *Glob J Health Sci* 2016; 8(10): 288.
 19. Borjali M, Amini-Rarani M, Nosratabadi M. Nonmedical Determinants of Congenital Heart Diseases in Children from the Perspective of Mothers: A Qualitative Study in Iran. *Cardiol Res Pract* 2021; 10
 20. Bahjati M, Modarresi V, Rahimpour S, Behjati MA. Congenital heart disease in the newborns of diabetic mothers: an echocardiographic evaluation. *J Shahid Sadoughi Univ Med Sci* 2011; 19(4): 511-7. [In Persian].
 21. Alyousif SMM, Aldokhel FT, Alkhanbashi OK, Alqahtani MHA, Aladawi AMM, Ashmawi AA, et al. The incidence of congenital heart defects in offspring among women with diabetes in Saudi Arabia. *Cureus* 2021; 13(3): e14225.
 22. Abu-Sulaiman RM, Subaih B. Congenital heart disease in infants of diabetic mothers: Echocardiographic study. *Pediatr Cardiol* 2004; 25(2): 137-40.