

Tissue Doppler Echocardiography: Assessment of the Cardiac Functions in Infant'S of Dia-betic Mothers

Amar Mohanrao Taksande

Amar Mohanrao Taksande, Department of Pediatrics, Jawaharlal Nehru Medical College, Wardha, India.

Conflict-of-interest statement: The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Correspondence to: Amar Mohanrao Taksande, Department of Pediatrics, Jawaharlal Nehru Medical College, Wardha, India.

Email: amar.taksande@gmail.com

Telephone: +07152-260310

Received: April 16, 2018

Revised: June 10, 2018

Accepted: June 15 2018

Published online: September 12, 2018

ABSTRACT

BACKGROUND: Diabetes in pregnancy is associated with an increased risk of complications in both the mother and fetus. Transient cardiac hypertrophy occurs in infants of diabetic mothers. Thus the aim of this study was to determine the changes in left ventricular function by Tissue Doppler echocardiography in an infant's of diabetic mothers.

MATERIAL AND METHODS: This was a case controlled study comprised of 15 infant of dia-betic mothers (cases) and 15 healthy term babies (controls). M-mode, Two-Dimensional, Doppler and Tissue Doppler Imaging measurements of cases and controls were performed.

RESULTS: There were 09 males and 06 females in the cases group. On cardiovascular examination, heart rate was 112 ± 12 beats per minute and blood pressure was $76 \pm 8.4/46 \pm 4.6$ mmHg in the cases. Both the left and right ventricle myocardial velocities were found to be lower in the infants of diabetic mothers compared to the control

group. The E'/A' ratio was found to be less than one in the left ventricle, right ventricular and septum in cases as compared to the control group. The Tei index of left ventricle was found to be higher in the infants of diabetic mothers (35.83 ± 8.23) who had a thicker interventricular septum compared to the control group (33.73 ± 8.23).
CONCLUSIONS: Tissue Doppler echocardiography is a useful, sensitive, non-invasive technique to study the changes in myocardial structure and function. The systolic and diastolic function indices measures are affected in babies of diabetic mothers as compare to normal neonates but not statistically significant.

Key words: Tissue Doppler Echocardiography; Diastolic function; Ventricular function; Infant of Diabetic Mother

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Taksande AM. Tissue Doppler Echocardiography: Assessment of the Cardiac Functions in Infant'S of Dia-betic Mothers. *Journal of Cardiology and Therapy* 2018; 5(1): 738-741 Available from: URL: <http://www.ghrnet.org/index.php/jct/article/view/2314>

INTRODUCTION

Fetal complications are directly related to inadequate glycemic control during important periods of pregnancy. Significant congenital disorders in the fetus, risk of premature delivery and increased prenatal morbidity and mortality are commonly occurred in Diabetic mother. Also it causes neonatal hypoglycemia, macrosomy and transient myocardial hypertrophy^[1,2]. Careful attention to pre-conception control of diabetes decreases the risk of anomalies. The high insulin level in the foetus and newborn may lead to disproportional septum thickening, left ventricular outlet stenosis, transient hypertrophic subaortic stenosis and heart failure in infant of diabetic mother (IDM)^[3,4]. IDMs with hypertrophic cardiomyopathy are recognized to have impaired myocardial performance, but less is known about ventricular function in IDMs without hypertrophy. Doppler echocardiography is used to assess the atrio-ventricular valve flow for the assessment of diastolic function. However, Tissue Doppler Imaging (TDI) is a type of Doppler ultrasound that records regional systolic and diastolic velocities within the myocardium and time to peak myocardial velocities with high temporal resolution. It can be used at any point of the ventricular myocardium to give information

on the regional wall motion. The measurement of both systolic and diastolic components can be made simultaneously with Tei index which is used for the evaluation of the ventricular functions^[6-9]. In IDM babies, systolic and diastolic functions of the heart have been studied by traditional echocardiography, but there are scanty number of studies conducted with Tissue Doppler Echocardiography (TDE). Hence the aim of our study was to assess the cardiac function of IDM babies by Tissue Doppler Echocardiography.

MATERIAL AND METHODS

This study was carried out in the Department of Pediatric, AVBRH hospital, Sawangi (Meghe), Wardha. It was a hospital based case-controlled study conducted from January 2016 to June 2017.

Inclusion criteria: (1) 15 IDM babies (cases); (2) 15 healthy term newborn(controls) who were born in the same hospital.

Exclusion criteria: Babies who had congenital heart disease, dysmorphic findings, birth asphyxia, prematurity, severe respiratory distress and critically ill neonates.

The study protocol was approved by the ethical institutional committee. Detailed general and systemic examination was done with special emphasis given for presence of heart murmur. By using Phillip echocardiography machine, two-dimensional (2D), M-mode, Doppler and Tissue Doppler Imaging was performed.

Echocardiographic examination

M-mode and two-dimensional echocardiography was done to measure the left ventricle internal dimensions including left ventricular internal dimension in diastole (LVIDd), left ventricle internal dimension in systole (LVIDs), Interventricular septal in diastole (IVSd) thickness, left ventricular posterior wall in diastole (LVPWd) thickness. The diameter of the aorta and left atrium was measured. The fractional shortening and ejection fraction was estimated using M-mode and Simpson in the parasternal long- and short-axis views as well as in the apical four-chamber view. Also, the apical four-chamber view was used to record LV inflow velocities in which the peak flow velocities of the LV inflow in early diastole (E) and late diastole with atrial contraction (A) were measured and E/A ratio was calculated. According to the American Society of Echocardiography recommendation, all the echocardiographic data were obtained.

TDI was performed in the apical four-chamber view by placing a sample volume at three different sites: (1) Lateral border of mitral valve annulus (Left Ventricle); (2) Interventricular Septum (IVS) and (3) Lateral border of tricuspid annulus (Right Ventricle). The peak systolic and diastolic velocities at the LV, RV and IVS were assessed with TDI in cases and controls. The following parameters were recorded: systolic velocity (S'), early diastolic velocity (E'), late diastolic velocity (A') and time intervals; isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT) and ejection time (ET) at each site. The IVRT was measured from the end of the S' wave to the onset of the E' wave, and the IVCT was measured from the end of the A' wave to the onset of the S' wave. The formula which was used to calculate the Tei index is as follow (Isovolemic contraction + isovolemic relaxation time/Ejection time)^[7-8].

Statistical analysis

All the data are expressed as mean \pm standard deviation (SD). The independent sample *t*-test was used to compare echocardiographic data between cases and controls. A value of $p < 0.05$ was considered statistically significant.

RESULTS

There were 09 males and 06 females in the cases. There was no significant difference in terms of birth weight (2870 ± 156 vs 2560 ± 243) and gestational week (38.24 ± 0.58 vs 38.05 ± 0.62) in cases as compared to the control group. On cardiovascular examination, heart rate was 112 ± 12 beats per minute and blood pressure was $76 \pm 8.4/46 \pm 4.6$ mmHg in the cases. On auscultation, two cases revealed an ejection systolic murmur heard maximally in 3rd left intercostal space parasternal area. No statistically significant differences were present between the M-mode echocardiographic measurements (LA, LVIVSd, LVIDd and LVPWd) for cases and controls as shown in Table 1. The ejection fraction and shortening fraction were lower in the cases than control, but the difference was not statistically significant. The LV Doppler of the mitral inflow velocity in IDMs showed higher E and A velocity and reduced E/A ratio as compared with control but not statistically significant. The S', E' and A' velocities of the left ventricle (LV), septum and right ventricle (RV) was lower but not statistically significant in the cases compared to the control group. The ratio of E' velocity to A' velocity (E'/A') in the LV, septum and RV was lower in cases as compared to the control group. This ratio was found to be lower than 1 in cases and control group as shown in Table 2. The Tei index of LV, septal and RV was found to be more in the babies of diabetic mothers as compared to control. Two patients had trivial tricuspid regurgitation without a significant pressure gradient.

DISCUSSION

The diabetes mellitus in mother may affect the structure and function of the fetal heart and alter the fetal placental circulation from embryonic development in the first trimester until the perinatal period through the second and third trimesters. Fetal hyperinsulinemia and increased affinity of insulin receptors, followed by changes in the metabolism of diabetic mothers, lead to alterations in cardiomyocyte gene expression and subsequent structural and functional heart malformation in the fetus. Zablah JE *et al*^[9] demonstrated that IDMs had significantly greater birth weight, lower gestational age, older maternal age, and higher incidence of maternal obesity and hypertension than normal neonates. In our study, there was no significant difference found in birth weight and gestational week in cases and control group. The most common heart malformations in fetuses include the following: transposition of great arteries, Truncus arteriosus, coarctation of the aorta, double outlet right ventricle, ventricular septal defect, hypoplastic left heart syndrome, and heterotaxy syndrome. Incidence of congenital heart defects among the IDMs is five times greater than that of the general population. While improvements in perinatal management have led to a reduction in diabetes-related mortality, the incidence of associated congenital anomalies remains higher than in the general population^[2-4]. Ciccone *et al*^[5] reported that with increasing gestational age, there were higher myocardial velocities and lower E/E' ratios and concluded that TDI addition to standard neonatal echocardiography may provide further important information about cardiac function.

The most common cardiac pathology in babies of diabetic mother is asymmetrical septal hypertrophy. There is an increased myocardial mass because of increased levels of insulin in these patients and lead to dysfunction in diastole^[9-10]. Most babies of diabetic mother may be asymptomatic despite diastolic dysfunction^[11]. The study done by Cooper *et al*^[12] reported 31% of septal hypertrophy in babies of diabetic mothers. On echocardiographic examination, findings of

Table 1 Standard Echocardiography parameters between cases and controls.

Echocardiography Parameter	Cases (Means ± SD)	Controls (Means ± SD)	P Value
M-Mode			
LA	8.73 ± 1.75	9.6 ± 2.12	0.87
LVIVSd	4.53 ± 1.06	4.01 ± 0.45	0.084
LVIDd	15.6 ± 1.72	14.93 ± 0.49	0.144
LVPWd	4.81 ± 0.86	4.46 ± 0.91	0.132
Shortening Fraction	37.01 ± 4.7	39.06 ± 3.72	0.062
2-Dimension			
Ejection Fraction	66.86 ± 3.88	68.93 ± 5.24	0.066
Doppler			
Mitral E (cm/s)	4.66 ± 0.72	4.62 ± 0.88	0.507
Mitral A (cm/s)	6.46 ± 1.47	5.43 ± 0.85	0.96
Mitral E/A	0.74 ± 0.15	0.86 ± 0.18	0.067

Table 2 TDI derived parameters between cases and controls.

TDI Parameter	Cases (Means ± SD)	Controls (Means ± SD)	P Value
TDI Lateral Mitral Annulus			
LV E'(cm/s)	3.62 ± 1.01	4.23 ± 1.52	0.143
LV A'(cm/s)	4.43 ± 1.42	5.02 ± 0.73	0.095
LV S'(cm/s)	3.86 ± 0.65	4.13 ± 0.32	0.108
LV E' / A'	0.87 ± 0.35	0.80 ± 0.23	0.755
LV Tei Index	35.83 ± 8.23	33.73 ± 8.23	0.245
TDI Interventricular Septum			
Septal E'(cm/s)	2.62 ± 0.72	3.24 ± 0.88	0.047
Septal A'(cm/s)	4.85 ± 2.43	4.42 ± 0.74	0.84
Septal S'(cm/s)	3.43 ± 0.56	3.54 ± 0.75	0.249
Septal E' / A'	0.57 ± 0.21	0.75 ± 0.29	0.058
Septal Tei Index	33.46 ± 3.81	30.26 ± 4.77	0.971
TDI Lateral Tricuspid Annulus			
RV E'(cm/s)	5.46 ± 1.30	9.33 ± 0.14	0.16
RV A'(cm/s)	7.01 ± 0.92	12.52 ± 1.87	0.132
RV S'(cm/s)	6.13 ± 2.11	9.23 ± 1.40	0.209
RV E' / A'	0.79 ± 0.19	0.74 ± 0.09	0.23
RV Tei Index	44.26 ± 5.44	40.26 ± 5.24	0.978

mainly asymmetrical septal hypertrophy, ventricular wall thickening and ventricular outlet obstruction may be observed.

TDI can measure the systolic and diastolic velocities within the myocardium of the ventricles. It is less dependent on loading conditions, and recently, applied more frequently for cardiac evaluation in fetuses. The study done by Nagueh *et al*^[13] found a significant decrease in the left ventricular E', A' and S' velocities in patients with hypertrophic cardiomyopathy. In our study, the left ventricular, septal and right ventricular E', A' and S' velocities were found to be lower in the cases as compared to the control group but not statistically significant. Notomi *et al*^[14] assessed the LV performance in healthy controls by measuring rotational mechanics with TDI and concluded that the LV performance increased significantly with age. The myocardial growth and an age-related increase in blood pressure may lead to greater myocardial velocities during systole in order to maintain adequate cardiac output. As E' represents myocardial tension in early diastole and the E' velocity is related with relaxation of the myocardium i.e. diastolic function. The variable E' is considered to indicate ventricular relaxation independent of volume load and reported diastolic dysfunction if E' value of < 8 cm/s^[15-16]. Mori *et al*^[17] found that the mean E' values

< 8 cm/s which was obtained from the left ventricle, right ventricle and septum of healthy newborns. Çimen D *et al*^[18] reported that the left and right ventricle myocardial velocities were lower in the babies of diabetic mothers compared to the control group, same finding were present in our study also. Zablath JE *et al*^[9] reported that babies of diabetic mother had significantly lower S' and E' velocities, at the MV, IVS, and TV than normal neonates. In adults, a S' velocity of > 5.4 cm/s in the mitral annulus indicates that ejection fraction is normal^[16]. In our study, the S' velocity for the right ventricle was found to be > 5.4 cm/s in the babies of diabetic mothers and control group.

On TDE, early findings of diastolic dysfunction are significant reduction in E', increase in A' velocities and reversal of the E'/A' ratio. Çimen D *et al*^[18] found that, the E'/A' ratio was below one only in the babies of diabetic mothers in the left ventricle in contrast to the control group. He also reported that, the E'/A' ratio in the septum and right ventricle was found to be below one both in the babies of diabetic mothers and control group. In our study, the left ventricular, septal and right ventricular E'/A' ratio was found less than one in babies of diabetic mothers and control group. These results showed that diastolic dysfunction was present in both ventricles in the cases and control group. Al-Biltagi M *et al*^[19] reported a significant deterioration of both systolic and diastolic functions measured by both conventional echocardiography and TDI in IDMs with both pre-gestational and gestational diabetes compared with the control group.

The Tei index is a variable which shows systolic and diastolic functions of the left and right ventricle. In the initial form of Tei index, pulsed Doppler was used^[20-21]. Subsequently, tissue Doppler was used for the measurements. The Tei index is a simple parameter for the evaluation of the RV and LV functions and is correlated with the invasive measurements of the cardiac systolic and diastolic functions^[11-13]. Çimen D *et al*^[18] found that the Tei index was higher in the babies of diabetic mothers who had a thicker IVS compared to the control group, similar finding was present in our study also. The fact that the Tei index was found to be significantly higher in babies of diabetic mothers than the control group was related with shortness of the ejection time and prolongation of isovolumic contraction time. These significant high values of the right and left ventricular Tei index show that LV functions were also affected in addition to RV dysfunction which may be observed in IDMs and which is attributed to physiological pulmonary hypertension^[18-22]. Al-Biltagi M *et al*^[19] concludes that TDI and two-dimensional STI were efficient and sensitive tools which were able to detect early cardiac dysfunction in babies of diabetic mothers even in the absence of morphologic cardiac changes.

Limitation of the Study

Small sample size was a main limitation of our study.

CONCLUSION

TDE is a useful, efficient and sensitive tool to study the changes in cardiac structure and function. The systolic and diastolic function indices measures are affected in babies of diabetic mothers as compare to normal neonates but not statistically significant.

REFERENCES

- Brans YW, Huff RW, Shannon DL, Hunter MA. Maternal diabetes and neonatal macro-somia. Postpartum maternal HbA1c levels and neonatal hypoglycemia. *Pediatrics* 1982; **70**: 576-81.
- Mormile R, Vittori G, De Michele M, Squarcia U, Quaini F.

- Postnatal regression of hyper-trophic cardiomyopathy in infants of diabetic- mothers: a crosstalk between Hox genes and epidermal growth factor (EGF) gene polymorphism? *Int J Cardiol* 2011; **150**: 340.
3. Sardesai MG, Gray AA, McGrath MM, Ford SE. Fetal hypertrophic cardiomyopathy in the fetus of a woman with diabetes. *Obstet Gynecol* 2001; **98**: 925-7. [PMID: 11704206]
 4. Tei C. New non-invasive index for combined systolic and diastolic ventricular function. *J Cardiol* 1995; **26**: 135-136. [PMID: 7674144]
 5. Ciccone MM, Scicchitano P, Zito A, Gesualdo M, Sassara M, Calderoni G et al. Different functional cardiac characteristics observed in term/preterm neonates by echocardiography and tissue doppler imaging. *Early Hum Dev*. 2011 Aug; **87(8)**: 555-8. [PMID: 21576005]; [DOI: 10.1016/j.earlhumdev.2011.04.012]
 6. Alam M, Witt N, Nordlander R, Samad BA. Detection of abnormal left ventricular function by Doppler tissue imaging in patients with a first myocardial infarction and showing normal function assessed by conventional echocardiography. *Eur J Echocardiogr* 2007; **1**: 37-41. [PMID: 17164098]; [DOI: 10.1016/j.euje.2005.12.012]
 7. Lopez L, Colan SD, Frommelt PC, Ensing GJ, Kendall K, Younoszai AK, Lai WW, Geva T. Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*. 2010; **23**: 465-495. quiz 576-467.
 8. Cui W, Roberson DA. Left ventricular Tei index in children: comparison of tissue Doppler imaging, pulsed wave Doppler, and M-mode echocardiography normal values. *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography*. 2006; **19**: 1438-1445. [PMID: 17138026]; [DOI: 10.1016/j.echo.2006.06.006]
 9. Zablah JE, Gruber D, Stoffels G, Cabezas EG, Hayes DA. Subclinical Decrease in Myocardial Function in Asymptomatic Infants of Diabetic Mothers: A Tissue Doppler Study. *Pediatr Cardiol*. 2017 Apr; **38(4)**: 801-806. [PMID: 28197645]; [DOI: 10.1007/s00246-017-1584-y]
 10. Deorari AK, Saxena A, Singh M, Shrivastava S. Echocardiographic assesment of infants born to diabetic mothers. *Arch Dis Child* 1989; **64**: 721-4.
 11. Thomas JD, Weyman AE. Echocardiographic Doppler evaluation of left ventricular diastolic function: Physics and physiology. *Circulation* 1991; **84**: 977-90. [PMID: 1884473]
 12. Cooper MJ, Enderlein MA, Tarnoff H, Roge CL. Asymmetric septal hypertrophy in infants of diabetic mothers. Fetal echocardiography and the impact of maternal diabetic control. *Am J Dis Child* 1992; **146**: 226-9.
 13. Nagueh SF, Bachinski LL, Meyer D, et al. Tissue Doppler imaging consistently detects myo-cardial abnormalities in patients with hypertrophic cardiomyopathy and provides a novel means for an early diagnosis before and independently of hypertrophy. *Circulation* 2001; **104**: 128-30.
 14. Notomi Y, Srinath G, Shiota T, Martin-Miklovic MG, Beachler L, Howell K et al. Maturational and adaptive modulation of left ventricular torsional biomechanics: Doppler tissue imaging observation from infancy to adulthood. *Circulation* 2006; **21**: 2534-41.
 15. Ichihashi K, Sato A, Shiraishi H, Momoi M. Tissue Doppler combined with pulsed-wave Doppler echocardiography for evaluating ventricular diastolic function in normal children. *Echocardiography* 2011; **28**: 93-6. [PMID: 20868441]; [DOI: 10.1111/j.1540-8175.2010.01279.x]
 16. Gulati VK, Katz WE, Follansbee WP, Gorcsan J. Mitral annular descent velocity by tissue doppler echocardiography as an index of global left ventricular function. *Am J Cardiol* 1996; **77**: 979-82.
 17. Mori K, Nakagawa R, Nii M, et al. Pulsed wave Doppler Tissue echocardiography assessment of the long axis function of the right and left ventricles during the early neonatal period. *Heart* 2004; **90**: 175-80. [PMID: 14729790]; [PMCID: PMC1768064]
 18. Çimen D, Karaaslan S. Evaluation of cardiac functions of infants of diabetic mothers using tissue Doppler echocardiography. *Turk Pediatri Ars* 2014; **49(1)**: 25-9.
 19. Al-Biltagi M(1), Tolba OA, Rowisha MA, Mahfouz Ael-S, Elewa MA. Speckle tracking and myocardial tissue imaging in infant of diabetic mother with gestational and pregestational diabetes. *Pediatr Cardiol*. 2015 Feb; **36(2)**: 445-53.
 20. Border WL, Michelfelder EC, Glascock BJ, et al. Color M-Mode and Doppler tissue evaluation of diastolic function in children: Simultaneous correlation with invasive indices. *J Am Soc Echocardiogr* 2003; **16**: 988-94. [PMID: 12931112]; [DOI: 10.1016/S0894-7317(03)00511-X]
 21. Tei C, Ling LH, Hodge DO, et al. New index of Combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. *J Cardiol* 1995; **26**: 357-66.
 22. Harada K, Orino T, Yasuoka K, Tamura M, Takada G. *Tohoku J Exp Med* 2000; **191**: 21-9.

Peer Reviewer: Pietro Scicchitano