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Assessment of cardiac diastolic function in infants of diabetic mothers using tissue Doppler echocardiography



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Abstract

Background: Limited number of studies evaluated cardiac diastolic function in infants of diabetic mothers using tissue Doppler imaging. The aim of this study was to evaluate diastolic parameters in full-term infants of diabetic mothers compared to healthy full-term neonates using both conventional echocardiography and tissue Doppler imaging. This study is a comparative study. Fifty consecutive infants of diabetic mothers (cases) in the first 3 days of life: 25 neonates with poor maternal glycemic control (Hemoglobin A1c > 7.5 g/dl) and 25 neonates with good maternal glycemic control (Hemoglobin A1c ≤ 7.5 g/dl). Thirty healthy full-term infants of non-diabetic mothers with age and sex matching were included as controls. The studied groups were assessed by conventional pulsed wave Doppler and tissue Doppler imaging.

Results: Among pulsed wave Doppler parameters, cases had lower values than controls as regards mitral E velocity, mitral E/A ratio, tricuspid E velocity, and tricuspid E/A ratio, while neonates with poor maternal glycemic control had lower values than those with good maternal glycemic control as regards mitral E/A ratio, tricuspid E velocity, and tricuspid E/A ratio as well as higher mitral A velocity (denoting more diastolic dysfunction). Similarly, among tissue Doppler parameters, cases had lower values than controls as regards septal E' velocity, E'/A' ratio, left ventricular E' velocity, E'/A' ratio, and right ventricular E' velocity as well as higher septal A' velocity, left ventricular A' velocity, and right ventricular A' velocity, while neonates with poor maternal glycemic control had lower values than those with good maternal glycemic control as regards septal E' velocity, E'/A' ratio, left ventricular E' velocity, E'/A' ratio, and right ventricular E' velocity, as well as higher left ventricular A' velocity (denoting more diastolic dysfunction). Tissue Doppler was able to detect higher number of neonates with left ventricular diastolic dysfunction than conventional pulsed wave Doppler.

Conclusions: Tissue Doppler imaging was found to be able to detect diastolic dysfunction early in infants of diabetic mothers specifically as regards the left ventricle. Tissue Doppler imaging should be considered an integral part of cardiac function assessment in infants of diabetic mothers.

Keywords: Diastolic dysfunction, Diastolic function, Infant of diabetic mother, Myocardial performance index, Tei index, Tissue Doppler imaging

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Background

The incidence of diabetes mellitus is increasing in the general population and a growing number of pregnancies are complicated by this condition [1]. Maternal diabetes mellitus negatively affects fetal condition by increasing risk of perinatal morbidity and mortality [2].

Cardiovascular abnormalities in infants of diabetic mothers occur either as congenital heart diseases (3–5%) or cardiomyopathy (10–20%). Fetal hyperinsulinism may trigger hyperplasia and hypertrophy of myocardial cells by increasing fat and protein synthesis [3].

Another study reported that asymmetrical septal hypertrophy is the most common cardiac pathology in infants of diabetic mothers [4].

Conventional pulsed wave Doppler measures diastolic flow across mitral and tricuspid valve. E wave velocity represents early passive diastolic flow caused by ventricular relaxation, while A-wave represents late active ventricular filling caused by atrial contraction in late diastole. Multiple factors affect conventional pulsed wave Doppler: heart rate, left atrial flow, and the influence of volume changes on trans-mitral flow. This makes the method inadequate for the diagnosis of diastolic dysfunction [5].

Tissue Doppler imaging is a non-invasive cardiac imaging technique, relatively independent on the loading conditions. It measures the velocity of the longitudinal motion of the mitral annulus, tricuspid annulus, and the basal part of inter-ventricular septum. Systolic wave (S') corresponds to ventricular ejection and E' wave reflects ventricular relaxation (elongation), while A' wave reflects atrial contraction and late ventricular filling. E' wave is the earliest marker of diastolic dysfunction and decreases with decreasing longitudinal lengthening (relaxation) in various pathological conditions [5].

Cardiac systolic and diastolic functions in infants of diabetic mothers have been studied by conventional echocardiography, but a limited number of studies were conducted using tissue Doppler echocardiography [4]. Moreover, a study performed using conventional echocardiography found that even normal neonates had bidirectional shunting across patent foramen ovale and patent ductus arteriosus in the first 12 h of life, a finding suggestive of elevated pulmonary pressure and right ventricular diastolic dysfunction [1].

The aim of this work was to assess the diastolic parameters in infants of diabetic mothers compared to healthy full-term neonates using both conventional echocardiography and tissue Doppler imaging. Within infants of diabetic mothers, the effect of glycemic control on cardiac diastolic function was also assessed using both conventional echocardiography and tissue Doppler imaging.

Methods

This study was a prospective comparative study conducted in the neonatal intensive care unit of a local governmental hospital in Port-Said governorate (Egypt) during 1-year period.

The study population was classified into two groups as follows: (1) Fifty consecutive full-term infants of diabetic mothers ("cases") in the first 3 days of age (excluding the first 12 h to allow for the physiological transitional period of neonatal circulation) and (2) Thirty healthy full-term infants of non-diabetic mothers with age and sex matching as controls. Diabetic mothers should have a known diagnosis of maternal type 1 or type 2 diabetes or gestational diabetes and were treated with diet alone, oral hypoglycemic drugs, or insulin therapy. Cases were further subdivided into 2 sub-groups: 25 infants of diabetic mothers with poor maternal glycemic control (hemoglobin A1c > 7.5 g/dl) and 25 infants of diabetic mothers with good maternal glycemic control (hemoglobin Aa1c ≤ 7.5 g/dl).

Neonates were excluded if there was maternal history of hypertension, preeclampsia, rheumatic heart disease, or drugs other than oral hypoglycemic drugs and insulin. Also, neonates were excluded if they were preterm (< 37 weeks gestational age), required mechanical ventilation, or suffered from major congenital malformations, perinatal asphyxia, chromosomal abnormalities, intrauterine growth retardation, neonatal sepsis, respiratory distress syndrome, suspected metabolic disorders, or suspected in utero infections.

Echocardiography was done by the same operator with previous experience in tissue Doppler and the same machine to avoid inter-observer errors. Echocardiography was performed for all cases and controls according to the recommendations of the American Society of Echocardiography [6] using SonoSite, M-turbo system with P10x 8-MHz transducer (multi-frequency transducer) (SonoSite Fujifilm Inc., Bothell WA, USA) with tissue velocity imaging capability. Electrocardiogram cables were simultaneously attached to the echocardiography machine and were used for timing of events in the cardiac cycle.

The following pulsed wave Doppler parameters were measured: peak E wave velocity, peak A wave velocity, and E/A ratio for the diastolic flow across mitral and tricuspid valves.

Tissue velocity imaging measures included systolic myocardial velocities (S') at the basal segments of the lateral left ventricular wall, septal wall, and right ventricular free wall, as well as early and late diastolic myocardial velocities and their ratio (E', A', and E'/A', respectively) of the same basal segments.

The Tei index (myocardial performance index) is a variable which shows systolic and diastolic functions of the left and right ventricle. Tei index was calculated (in tissue Doppler imaging) as the sum of isovolumic

contraction time and isovolumic relaxation time divided by ventricular ejection time [7]. All interval measurements were performed within the same cardiac cycle. Isovolumic contraction time was defined as the time duration between the beginning of QRS complex in the electrocardiogram and the beginning of S' wave. The isovolumic relaxation time was defined as the interval between the end of S' wave and the beginning of the E' wave of the next cardiac cycle.

All measurements (being affected by respiration) were repeated along five consecutive cardiac cycles, and the mean value of each parameter was recorded and these mean values were used for statistical calculations.

Statistical analysis

All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS version 17 statistical program (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA). A probability value (p value) less than 0.05 was considered statistically significant.

All comparisons between two groups were performed using Student's t test. Chi-squared test (χ^2) was used to define associations between non-parametric categorical variables. Fisher's exact test was used instead when the expected frequency is less than 5.

Results

Our cases (including those with poor maternal glycemic control and those with good maternal glycemic control) and controls had gestational age (weeks) 37.6 ± 0.5 , 37.3 ± 0.53 , and 37.7 ± 0.46 respectively, age (days) 3.56 ± 1.2 , 3.64 ± 1.2 , and 3.63 ± 1.2 respectively, maternal age (years) 26.24 ± 3 , 26 ± 3.3 , and 25.73 ± 3 respectively, all with statistically non-significant differences. Sex distribution in both groups (cases and controls) did not show statistically significant difference.

Maternal diabetes was gestational in 20 mothers (80%) among those with poor glycemic control and in 21 (84%) among those with good control. Chronic diabetes was present in 5 mothers (20%) in the poor control group and in 4 (16%) in the good control group. This had no statistical significance.

All neonates had no respiratory distress or only minimal distress that improved within the first few hours with conservative management. Heart rate was within the normal range in all studied neonates.

Among cases, 20 infants of diabetic mothers (80%) were large for gestational age in the poor glycemic control group compared to only 2 (8%) in the good control group with statistically significant difference ($p < 0.001$).

Blood glucose level was done as a routine hospital policy in any infant of diabetic. Newborns with poor maternal glycemic control had significantly lower blood

glucose levels compared to those with good maternal control (37.4 ± 4.5 g/dl vs. 57.8 ± 7.4 g/dl respectively, $p < 0.001$). Blood glucose returned to normal levels in all hypoglycemic neonates with routine management within the first 12 h (i.e., before echocardiography was done).

Among pulsed wave Doppler parameters, cases showed more evidence of diastolic dysfunction as they had statistically significant lower values than controls as regards mitral E velocity ($p < 0.001$), mitral E/A ratio ($p < 0.001$), tricuspid E velocity ($p = 0.001$), and tricuspid E/A ratio ($p = 0.001$), while there was no significant difference as regards mitral A velocity and tricuspid A velocity (Table 1).

Similarly, among tissue Doppler parameters, cases showed more evidence of diastolic dysfunction as they had statistically significant lower values than controls as regards septal E' velocity ($p = 0.001$), E'/A' ratio ($p < 0.001$), left ventricular E' velocity ($p < 0.001$), and E'/A' ratio ($p < 0.001$) as well as right ventricular E' velocity ($p = 0.001$) and statistically significant higher septal A' velocity ($p = 0.019$), left ventricular A' velocity ($p < 0.001$) and right ventricular A'

Table 1 Comparison between cases and control groups as regards PW Doppler, TDI, and TDI-based MPI

Parameter	Cases (n = 50)	Control (n = 30)	p
M-E	53.3 ± 6.5	68.2 ± 7.8	< 0.001*
M-A	61.5 ± 6.4	59.8 ± 8.3	0.31
M-E/A	0.87 ± 0.08	1.1 ± 0.12	< 0.001*
T-E	47.5 ± 5.3	52.9 ± 8.3	0.001*
T-A	61.2 ± 7.3	60.1 ± 6.5	0.51
T-E/A	0.79 ± 0.12	0.88 ± 0.12	0.001*
IVS-E'	4.4 ± 0.5	5 ± 0.8	0.001*
IVS-A'	5.43 ± 0.7	5.1 ± 0.4	0.019*
IVS-S'	4.15 ± 0.7	3.85 ± 0.9	0.086
IVS-E'/A'	0.81 ± 0.1	0.99 ± 0.2	< 0.001*
LV-E'	5.4 ± 0.6	7.2 ± 1.2	< 0.001*
LV-A'	7.2 ± 0.8	6.1 ± 0.9	< 0.001*
LV-S'	4.77 ± 0.5	4.8 ± 0.7	0.72
LV-E'/A'	0.77 ± 0.13	1.2 ± 0.26	< 0.001*
RV-E'	6.17 ± 0.76	7.1 ± 1.5	0.001*
RV-A'	7.65 ± 0.92	8.4 ± 1.7	0.04*
RV-S'	6.2 ± 0.96	6.7 ± 1.2	0.09
RV-E'/A'	0.81 ± 0.1	0.86 ± 0.16	0.18
IVS-MPI	0.46 ± 0.05	0.37 ± 0.04	< 0.001*
LV-MPI	0.48 ± 0.06	0.38 ± 0.04	< 0.001*
RV-MPI	0.44 ± 0.04	0.35 ± 0.04	< 0.001*

*Statistically significant, velocities in centimeters/second
PW pulsed wave, CW continuous wave, M mitral, T tricuspid, E E wave velocity, A A wave velocity, IVS septal, LV left ventricular, RV right ventricular, E' E' wave velocity, A' A' wave velocity, S' S' wave velocity, TDI tissue Doppler imaging, MPI myocardial performance index (Tei Index)

velocity ($p = 0.040$), while there was no significant difference in other parameters (Table 1).

Among tissue Doppler-based Tei index parameters, cases had statistically significant higher values than controls as regards septal ($p < 0.001$), left ventricular ($p < 0.001$), and right ventricular ($p < 0.001$) myocardial performance indices (Table 1) denoting more global and diastolic dysfunction.

Within infants of diabetic mothers, the effect of glycemic control on cardiac diastolic function was assessed. Among pulsed wave Doppler parameters, infants of diabetic mothers with poor maternal glycemic control had more evidence of diastolic dysfunction as they had statistically significant lower values than those with good maternal glycemic control as regards mitral E/A ratio ($p < 0.001$), tricuspid E velocity ($p = 0.041$), and tricuspid E/A ratio ($p = 0.005$), as well as statistically significant higher mitral A velocity ($p = 0.032$), while there was no significant difference as regard mitral E velocity and tricuspid A velocity (Table 2).

Table 2 Comparison between cases with poor vs. good maternal glycemic control as regards PW-Doppler, TDI, and TDI-based MPI

Parameter	Poor control (n = 25)	Good control (n = 25)	p
M-E	52.5 ± 6	54.1 ± 6.9	0.38
M-A	63.4 ± 5.5	59.6 ± 6.7	0.032*
M-E/A	0.83 ± 0.07	0.9 ± 0.06	< 0.001*
T-E	46 ± 5.6	49 ± 4.6	0.041*
T-A	62.8 ± 7	59.6 ± 7.3	0.12
T-E/A	0.74 ± 0.1	0.83 ± 0.1	0.005*
IVS-E'	4.2 ± 0.33	4.5 ± 0.58	0.03*
IVS-A'	5.4 ± 0.6	5.4 ± 0.8	0.81
IVS-S'	4 ± 0.66	4.3 ± 0.64	0.13
IVS-E'/A'	0.78 ± 0.1	0.84 ± 0.08	0.03*
LV-E'	5 ± 0.46	5.8 ± 0.5	< 0.001*
LV-A'	7.6 ± 0.8	6.7 ± 0.5	< 0.001*
LV-S'	4.78 ± 0.5	4.77 ± 0.5	0.97
LV-E'/A'	0.66 ± 0.08	0.87 ± 0.08	< 0.001*
RV-E'	6 ± 0.87	6.4 ± 0.57	0.049*
RV-A'	7.5 ± 0.94	7.8 ± 0.9	0.32
RV-S'	6.2 ± 1	6.2 ± 0.9	0.87
RV-E'/A'	0.79 ± 0.11	0.82 ± 0.1	0.3
IVS-MPI	0.47 ± 0.04	0.45 ± 0.05	0.23
LV-MPI	0.49 ± 0.05	0.47 ± 0.07	0.23
RV-MPI	0.45 ± 0.04	0.43 ± 0.04	0.27

*Statistically significant, velocities in centimeters/second
 PW pulsed wave, CW continuous wave, M mitral, T tricuspid, E E wave velocity, A A wave velocity, IVS septal, LV left ventricular, RV right ventricular, E' E' wave velocity, A' A' wave velocity, S' S' wave velocity, TDI tissue Doppler imaging, MPI myocardial performance index (Tei Index)

Similarly, among tissue Doppler parameters, infants of diabetic mothers with poor maternal glycemic control had more evidence of diastolic dysfunction as they had statistically significant lower values than those with good maternal glycemic control as regards septal E' velocity ($p = 0.030$), E'/A' ratio ($p = 0.030$), left ventricular E' velocity ($p < 0.001$), E'/A' ratio ($p < 0.001$), and right ventricular E' velocity ($p = 0.49$), as well as statistically significant higher left ventricular A' velocity ($p < 0.001$), while there was no significant difference in other parameters (Table 2).

Among tissue Doppler-based Tei index parameters, there were no significant differences between infants of diabetic mothers with poor maternal glycemic control and those with good maternal glycemic control as regards all parameters (Table 2).

Cases showed statistically significant higher incidence of left ventricular diastolic dysfunction than controls in both pulsed wave Doppler (defined as E/A ratio < 1) and tissue Doppler (defined as E'/A' ratio < 1) with $p < 0.001$ and $p < 0.001$ respectively, while there was no difference as regards right ventricular diastolic dysfunction (Table 3). Tissue Doppler was able to detect left ventricular diastolic dysfunction in higher number of neonates than conventional pulsed wave Doppler (40 out of 50 cases and 6 out of 30 controls by tissue Doppler compared to 28 out of 50 cases and 1 out of 30 controls by conventional pulsed wave Doppler respectively).

Moreover, regarding the effect of maternal glycemic control, infants of diabetic mothers with poor maternal glycemic control showed statistically significant higher incidence of left ventricular diastolic dysfunction than those with good maternal glycemic control in both pulsed wave Doppler (defined as E/A ratio < 1) and tissue Doppler (defined as E'/A' ratio < 1) with $p = 0.023$ and $p = 0.001$ respectively, while there was no difference as regards right ventricular diastolic dysfunction (Table 4). Again, tissue

Table 3 Comparison between cases and controls as regards diastolic dysfunction

Diastolic dysfunction		Cases (n = 50)	Control (n = 30)	p
Pulsed wave Doppler				
RV-DD	Present	41	19	0.11
	Absent	9	11	
LV-DD	Present	28	1	< 0.001*
	Absent	22	29	
Tissue Doppler imaging				
RV-DD	Present	38	17	0.071
	Absent	12	13	
LV-DD	Present	40	6	< 0.001*
	Absent	10	24	

*Statistically significant
 RV-DD right ventricular diastolic dysfunction, LV-DD left ventricular diastolic dysfunction

Table 4 Comparison between cases with poor vs. good maternal glycemic control as regards diastolic dysfunction

Diastolic dysfunction		Poor control (n = 25)	Good control (n = 25)	p
Pulsed wave Doppler				
RV-DD	Present	22	19	0.46
	Absent	3	6	
LV-DD	Present	18	10	0.023*
	Absent	7	15	
Tissue Doppler imaging				
RV-DD	Present	21	17	0.32
	Absent	4	8	
LV-DD	Present	25	15	0.001*
	Absent	0	10	

*Statistically significant

RV-DD right ventricular diastolic dysfunction, LV-DD left ventricular diastolic dysfunction

Doppler was able to detect left ventricular diastolic dysfunction in higher number of neonates than conventional pulsed wave Doppler (all 25 cases with poor control and 15 out of 25 cases with good control by tissue Doppler compared to 18 out of 25 cases with poor control and 10 out of 25 cases with good control by conventional pulsed wave Doppler respectively).

Discussion

Deorari et al. [8] mentioned that the most common cardiac pathology in babies of diabetic mothers is asymmetrical septal hypertrophy which might lead to dysfunction in diastole. However, most babies of diabetic mothers may be asymptomatic despite this dysfunction [9]. That was clear in the work of Vural et al. [10] who found that symptomatic hypertrophic cardiomyopathy occurs in 12.1% of infants of diabetic mothers and the prevalence increases to 40% when routinely searched for with echocardiography.

The results of the study conducted by Arslan et al. [11] match ours. They found statistically significant differences in pulsed wave Doppler with lower mitral E velocity, mitral E/A ratio, and tricuspid E velocity in infants of diabetic compared to those of controls ($p < 0.0001$, $p < 0.0001$, and $p = 0.049$ respectively). In addition, they found statistically significant higher mitral A velocity in cases than in the control group ($p = 0.002$).

E' velocity (measured by tissue Doppler imaging) is considered to be a variable which indicates ventricular relaxation independent of volume load. One of the early stage findings of diastolic dysfunction is significant reduction in E' velocity and increase in A' velocity in tissue Doppler imaging which leads to reversal of the E'/A' ratio (i.e., to become < 1) [12].

It was previously well established that patients with hypertrophic cardiomyopathy suffer a significant

reduction in the left ventricular E', A', and S' velocities [13]. In addition, Lopez et al. [14] declared that impairment of left ventricular and right ventricular relaxation results in the decrease E' wave velocity.

Arslan et al. [11] also stated that during analysis of tissue Doppler imaging parameters from left ventricle, right ventricle, and inter-ventricular septum, they found lower E' wave velocity ($p < 0.0001$, $p < 0.001$, and $p = 0.031$ respectively), higher A' wave velocity ($p = 0.004$, $p = 0.009$, and $p = 0.042$ respectively), and lower E'/A' ratio ($p < 0.0001$, $p < 0.0001$, and $p = 0.044$ respectively) in infants of diabetic mothers compared to controls. This matches our results and is attributed to a reduced ventricular relaxation.

The results of the study of Çimen and Karaaslan [4] also match our results to a great extent. The E' velocities in the right ventricle, left ventricle, and septum were significantly lower in the babies of diabetic mothers compared to the control group ($p = 0.001$, $p = 0.001$, and $p = 0.001$ respectively). In addition, the A' velocities in the right ventricle, left ventricle, and septum were significantly higher in the babies of diabetic mothers compared to the control group ($p = 0.001$, $p = 0.001$, and $p = 0.001$ respectively). E'/A' ratios in the right and left ventricles were significantly lower in the babies of diabetic mothers compared to the control group ($p = 0.025$ and $p = 0.030$ respectively).

Moreover, Al-Biltagi et al. [15] found significant deterioration of left ventricular diastolic function measured by both conventional echocardiography (E/A ratio) and tissue Doppler imaging (E'/A' ratio) with $p < 0.0001$ and $p < 0.0001$ respectively among cases (infants of diabetic mothers) compared to the control group. They also found a significant deterioration of right ventricular diastolic function measured by tissue Doppler imaging (E'/A' ratio) with $p < 0.0001$ in cases compared to controls.

The Tei index [7] was initially measured by pulsed Doppler in the past and subsequently using tissue Doppler [16]. It is a useful parameter for indicating systolic and diastolic functions [14]; because it is a simple, reproducible and non-invasive index that has close correlation with systolic and diastolic hemodynamic parameters has the potential in the clinical field for the assessment of global cardiac performance.

Again, in accordance with our results, Tei index in the left ventricle, right ventricle, and the inter-ventricular septum were statistically higher ($p < 0.0001$, $p = 0.044$, and $p = 0.001$ respectively) in cases than in controls in the study of Arslan et al. [11] denoting impairment of global myocardial performance in cases.

Similarly, left ventricular and right ventricular Tei indices were higher in infants of diabetic mothers whose mothers had either gestational or pre-gestational diabetes than in healthy control infants in the study of

Çimen and Karaaslan [4] ($p = 0.015$ and $p = 0.005$ respectively) as well as the study conducted by Al-Biltagi et al. [15] ($p = 0.0004$ and $p = 0.0002$ respectively).

Previously, Tsutsumi et al. [17] also found an increased left ventricular and right ventricular Tei index in fetuses of diabetic mothers after 27 weeks.

The increased left ventricular, right ventricular, and septal Tei indices in the newborns of diabetic mothers indicated impairment of the global ventricular function. These significantly high values of the right and left ventricular Tei indices show that left ventricular functions were also affected in addition to right ventricular dysfunction which could be attributed to physiological pulmonary hypertension (elevated pulmonary vascular resistance) in the early neonatal period.

Another important target in our study was to evaluate the effect of maternal diabetes control on echocardiographic parameters in infants of diabetic mothers.

Sub-optimally controlled diabetes (associated with higher levels of glucose during gestation) leads to hyperinsulinemia which increases leptin and free fatty acids transfer leading to macrosomia [18–20].

El-Ganzoury et al. [21] found in their study that all infants with hypertrophic cardiomyopathy were born to mothers with sub-optimally controlled diabetes and 86.6% of them were large for gestational age. Moreover, all small for gestational age and large for gestational age neonates in their study were born to mothers with sub-optimally controlled diabetes, while 88% of appropriate for gestational age neonates were born to mothers with optimal metabolic control. These data highlight the impact of good maternal diabetic control.

Similarly, other studies had shown an association between poor maternal glycemic control and asymmetrical septal hypertrophy [22–24].

On the contrary, other studies noted that even strict glycemic control does not efficiently prevent the fetuses of diabetic mothers from abnormal cardiac growth [25, 26].

Kozak-Barany et al. [27] showed that infants of mothers with well-controlled pre-gestational or gestational diabetes had impaired left ventricular relaxation. They related this finding to the effects of maternal hyperglycemia during the third trimester and subsequent fetal hyperinsulinemia leading to neonatal cardiac hypertrophy.

Also, Ren et al. [28] found that diastolic filling abnormalities are present in pregnancies with good diabetic control and they were more evident in pregnancies with poor glycemic control. Fetal E values in pulsed wave Doppler and the E/A ratio were significantly lower in pregnancies with uncontrolled gestational diabetes mellitus.

As noted previously, our group of infants of diabetic mothers with poor maternal glycemic control showed

statistically significant higher incidence of left ventricular diastolic dysfunction than those with good maternal glycemic control in both pulsed wave Doppler (defined as E/A ratio < 1) and tissue Doppler (defined as E'/A' ratio < 1), while there was no difference as regards the incidence of right ventricular diastolic dysfunction. However, as regards tissue Doppler-based Tei index parameters, we could not demonstrate significant differences between infants of diabetic mothers with poor maternal glycemic control and those with good maternal glycemic control. This highlights two facts: first, global myocardial function is affected in both categories and second, and most important, is that assessment of myocardial function is important in newborns of diabetic mothers regardless the degree of maternal glycemic control.

Roodpeyma et al. [29] showed that the somatic findings of newborns were not related to the occurrence of cardiac complications. The relation between increased somatic growth and cardiac dysfunction could be only that both are attributable to the same mechanism. Insulin resistance-associated hyperinsulinemia (frequently associated with pregnancy-associated diabetes) can induce smooth muscle cell hypertrophy and hyperplasia and increased extracellular proteins which contributes to increase birth weight and at the same time affect the cardiac function [30].

In the present work, left ventricular diastolic dysfunction in individual neonates was detected more with tissue Doppler than with conventional pulsed wave Doppler. This fact highlights the importance of tissue Doppler imaging (if available) in detecting diastolic dysfunction as many cases would be missed by conventional pulsed wave Doppler alone.

We focused in the present study on the occurrence of diastolic dysfunction and not just a hypertrophied interventricular septum because the finding of diastolic dysfunction is more important and more related to the clinical status than septal hypertrophy per se.

Limitations of the study

Tissue Doppler imaging has its own limitations which are encountered in any study relying on this modality of echocardiography. Tissue Doppler imaging measures only motion that is parallel to the direction of the ultrasound beam. In addition, active motion of the myocardium cannot be surely differentiated from passive motion of the heart inside the thorax.

Our study has certain limitations such as relatively small number of cases in the studied subgroups and lack of follow-up period. We did not do speckle-tracking as it was not available in the area where the study was done and transfer of such neonates to specialized echocardiography laboratory carries its own hazards.

Conclusion

Infants of diabetic mothers (compared to normal controls) have more evidence of diastolic dysfunction in both conventional pulsed wave Doppler and tissue Doppler imaging and more global impairment of ventricular function (Tei index) measured by tissue Doppler imaging. Moreover, infants of diabetic mothers with poor maternal glycemic control (compared to those with good control) have more evidence of diastolic dysfunction in both conventional pulsed wave Doppler and tissue Doppler imaging.

Tissue Doppler imaging is able to detect left ventricular diastolic dysfunction more precisely than conventional pulsed wave Doppler in such peculiar group of neonates. Hence, tissue Doppler imaging (if available) should be considered an integral part in the assessment of cardiac function in infants of diabetic mothers.

Abbreviations

A wave: Late diastolic flow velocity in pulsed wave Doppler; A' wave: Late diastolic myocardial velocity in tissue Doppler imaging; E wave: Early diastolic flow velocity in pulsed wave Doppler; E' wave: Early diastolic myocardial velocity in tissue Doppler imaging; E/A ratio: Ratio of early-to-late diastolic flow velocities in pulsed wave Doppler; E'/A' ratio: Ratio of early-to-late diastolic myocardial velocities in tissue Doppler imaging; S' wave: Systolic myocardial velocity in tissue Doppler imaging

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Authors' contributions

AAS designed the study, performed echocardiography, and wrote and submitted the manuscript. MMAS shared in the study design, supervised and coordinated the whole work, and critically revised the final version of the manuscript. RKA coordinated the sample collection, collected clinical data, and helped in drafting the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated during the current study are not publicly available due to hospital policies and because the data of controls will be used in future research to generate normal tissue Doppler values in Egyptian neonates (as part of normal values in the first year of age), but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guides on the care and has been approved by the ethical committee in Al-Azhar University, Cairo, Egypt (reference number is not available). Parental consents were obtained verbally.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

- Katheria A, Leone T (2012) Altered transitional circulation in infants of diabetic mothers with strict antenatal obstetric management: a functional echocardiography study. *J perinatol* 32:508–513
- Chu C, Gui YH, Ren YY et al (2012) The impacts of maternal gestational diabetes mellitus (GDM) on fetal hearts. *Biomed Environ Sci* 25:15–22
- Korraa A, Ezzat MH, Bastawy M et al (2012) Cardiac troponin I levels and its relation to echocardiographic findings in infants of diabetic mothers. *Ital J Pediatr* 38:39
- Çimen D, Karaaslan S (2014) Evaluation of cardiac functions of infants of diabetic mothers using tissue Doppler echocardiography. *Türk Ped Arş* 49: 25–29
- Mitrovska S, Jovanova S, Lazeska B (2014) Tissue Doppler imaging in the early detection of diastolic dysfunction in asymptomatic diabetic patients. *Clin Cardiol Res* 1(1):4
- Lai WW, Geva T, Shirali GS et al (2006) Guidelines and standards for performance of a pediatric echocardiogram: a report from the task force of the pediatric council of the American Society of Echocardiography. *J Am Soc Echocardiogr* 19:1413–1430
- Tei C, Ling LH, Hodge DO et al (1995) 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* 26:357–366
- Deorari AK, Saxena A, Singh M et al (1989) Echocardiographic assessment of infants born to diabetic mothers. *Arch Dis Child* 64:721–724
- Thomas JD, Weyman AE (1991) Echocardiographic Doppler evaluation of left ventricular diastolic function: Physics and physiology. *Circulation* 84: 977–990
- Vural M, Leke L, Mahomedaly H et al (1995) Should an echocardiographic scan be done routinely for infants of diabetic mothers? *Turk J Pediatr* 37(4): 351–356
- Arslan D, Oran B, Vatansev H et al (2013) The usefulness of plasma asymmetric dimethylarginine (ADMA) levels and tissue Doppler echocardiography for heart function in term infants born to mothers with gestational diabetes mellitus. *J Matern Fetal Neonatal Med* 26(17): 1742–1748
- Ichihashi K, Sato A, Shiraishi H et al (2011) Tissue Doppler combined with pulsed-wave Doppler echocardiography for evaluating ventricular diastolic function in normal children. *Echocardiography* 28:93–96
- Nagueh SF, Bachinski LL, Meyer D et al (2001) Tissue Doppler imaging consistently detects myocardial abnormalities in patients with hypertrophic cardiomyopathy and provides a novel means for an early diagnosis before and independently of hypertrophy. *Circulation* 104:128–130
- Lopez L, Colan SD, Frommelt PC et al (2010) 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. *J Am Soc Echocardiogr* 23:465–495
- Al-Biltagi M, Tolba OARE, Rowisha MA et al (2015) Speckle tracking and myocardial tissue imaging in infant of diabetic mother with gestational and pre-gestational diabetes. *Pediatr Cardiol* 36:445–453
- Harada K, Orino T, Yasuoka K et al (2000) Tissue Doppler imaging of left and right ventricles in normal children. *Tohoku J Exp Med* 191:21–29
- Tsutsumi T, Ishii M, Eto G et al (1999) Serial evaluation for myocardial performance in fetuses and neonates using a new Doppler index. *Pediatr Int* 41:722–727
- Taylor R, Lee C, Kyne-Grzebalski D et al (2002) Clinical outcomes of pregnancy in women with type 1 diabetes. *Obstet Gynecol* 99:537–541
- Butte NF (2000) Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus. *Am J Clin Nutr* 71(Suppl. 5): 1256S–1261S
- Mehta A, Hussain K (2003) Transient hyperinsulinism associated with macrosomia, hypertrophic obstructive cardiomyopathy, hepatomegaly and nephromegaly. *Arch Dis Child* 88:822–824

21. El-Ganzoury MM, El-Masry SA, El-Farrash RA et al (2012) Infants of diabetic mothers: echocardiographic measurements and cord blood IGF-I and IGFBP-1. *Pediatr Diabetes* 13:189–196
22. Ulmo S, Vial Y, Di Bernardo S et al (2007) Pathologic ventricular hypertrophy in the offspring of diabetic mothers: a retrospective study. *Eur J heart* 28: 1319–1325
23. Narchi H, Kulaylat N (2000) Heart disease in infants of diabetic mothers. *Images Paediatr Cardiol* 3:17–23
24. Czeszyńska MB, Dawid G, Konefal H et al (2004) Cord blood leptin, insulin, C-peptide, IGF-1 and IGF-2 levels in relation to echocardiographic measurements in infants of diabetic mothers: preliminary report. *Med Sci Mon* 10(Suppl. 2):28–32
25. Aman J, Hansson V, Ostlund I et al (2011) Increased fat mass and cardiac septal hypertrophy in newborn infants of mothers with well-controlled diabetes during pregnancy. *Neonatology* 100(2):147–154
26. Garcia-Flores J, Janez M, Gonzalez MC et al (2011) Fetal myocardial morphological and functional changes associated with well-controlled gestational diabetes. *Eur J Obstet Gynecol Reprod Biol* 154:24–26
27. Kozak-Barany A, Jokinen E, Kero P et al (2004) Impaired left ventricular diastolic function in newborn infants of mothers with pregestational or gestational diabetes with good glycemic control. *Early Hum Dev* 77(1–2): 13–22
28. Ren Y, Zhou Q, Yan Y et al (2011) Characterization of fetal cardiac structure and function detected by echocardiography in women with normal pregnancy and gestational diabetes mellitus. *Prenat Diagn* 31:459–465
29. Roodpeyma S, Rafieyan S, Khosravi N et al (2013) Cardiovascular complications in infants of diabetic mothers: an observational study in a Pediatric Cardiology Clinic in Tehran. *J Compr Ped* 3(3):120–123
30. Nigro J, Osman N, Dart AM et al (2006) Insulin resistance and atherosclerosis. *Endocr Rev* 27(3):242–259

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