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Ductus Venosus Doppler Ultrasound in Diabetic Pregnancies

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Abstract
With the increased prevalence of diabetic pregnancies, it is necessary to develop a simple reliable method for screening of the fetal cardiovascular system, which is a potential site for adverse effects due to maternal hyperglycemia. Being an easy tool, the ductus venosus Doppler velocities might be an appropriate method. This is a cross section clinical observation study conducted in Damietta General Hospital. Study included 100 *diabetic pregnant women during their third trimester (cases) and* 100 *women with normal pregnancy as control. Each patient was submitted to detailed history taking, clinical examination, and Doppler ultra sonographic assessment of ductus venosus.* ***Results:*** *The diabetic mothers had higher BMI, infants with larger birth weight and low 5-minute Apgar score. Regarding ductus venosus (DV) Doppler assessment. There was a significant elevation of all DV indices among cases than controls including pulsatility index, preload index and peak velocity index for the vien. Poor control of diabetes was associated with elevated all DV indices among diabetic cases of the study. Also, pre-gestational DM was associated with significantly higher pulsatility index and preload index. Newborns with low 5-min Apgar score had significantly higher plasticity index and preload index than newborns with normal 5-min Apgar score. Diabetic pregnancies demonstrated significant difference of ductus venosus Doppler parameters compared with non-diabetic controls, possibly indicating a fetal cardiac effect.*

Keywords: *Diabetes mellitus, ductus venosus*

Introduction
Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (ADA, 2016). It is one of the most common non-communicable diseases, with serious consequences (Ahmed et al., 2015). DM may be classified as type 1 diabetes, associated with pancreatic failure and insulin deficiency; type 2 diabetes, associated with ineffective insulin utilization; or gestational diabetes mellitus (GDM), which is diabetes first diagnosed or recognized in pregnancy (Lyons, 2015).

Diabetes in pregnancy is associated with frequent adverse perinatal outcomes including congenital malformations, perinatal mortality, preterm delivery and large for gestational age (LGA) infants (McCance, 2015). Fetal anomalies predominantly involve cardiovascular anomalies, which comprises the highest proportion and are the greatest contributor to perinatal mortality (Miller et al., 2013). The ductus venosus (DV) is a blood vessel, unique to the fetal circulation that originates from the umbilical vein (UV) and enters the inferior vena cava at the inlet to the right atrium (Dahlback et al., 2016). Abnormal DV waveforms could be a consequence of delayed maturation of the cardiovascular system, fetal chromosomal abnormalities without cardiac malformations, cardiac dysfunction from congenital cardiac anomalies, or fetal growth restriction (Suksai et al., 2016). The DV waveform reflects the pressure–volume changes in the heart. Despite the limited specificity of the DV waveform, its correlation with cardiac forward function makes it of central importance in assessing the overall severity of fetal cardiovascular pathology (Seravalli et al., 2016).

In recent years, DV Doppler velocities, DV velocity ratios, and diastolic time intervals have been used to evaluate fetal cardiac function and well-being in complicated pregnancies, including gestational diabetes (Avcı et al., 2016). Diabetic pregnancies might exhibit abnormal DV hemodynamics; hence it may indicate modified fetal cardiac function (Stuart et al., 2010).

Patients and methods
This is a cross section clinical observation study conducted in Damietta General Hospital. It included 100 diabetic pregnant women during their third trimester (cases) and 100 women with normal pregnancy as control. Fetuses with IUGR or suspected chromosomal anomalies were excluded from the study. Mothers with disorders affecting cardiovascular system as hypertension, collagen and renal diseases were also excluded. Follow up: each patient was followed until delivery and the following data regarding newborns were obtained: Apgar score at 1 and 5 minutes, birth weight. Large for gestational age (LGA) are those with birth weight > the 80th percentile for gestational age.

Appropriate for gestational age (AGA) are newborns with birth weight between 10th and 80th percentiles. According to Wong et al. (2010), adverse perinatal outcome was defined as1-min Apgar score < 4 or 5-min Apgar score < 7. Routine examination of newborns revealed that there were no apparent congenital anomalies. Ultrasound scan: Ultrasound scan was performed (Idris et al., 2010). Umbilical artery blood velocities were recorded from the mid-portion of the umbilical cord. The umbilical artery PI was calculated automatically by the ultrasound systems according to the method of Gosling et al. (1971). Ethical consent: The nature of the study was clearly explained to each patient. An informed written consent was obtained.

Statistical analysis

The collected data were organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 19 (SPSS Inc, Chicago, USA), running on IBM compatible computer . Quantitative data were expressed as the mean ± standard deviation (SD). Qualitative data were presented as relative frequency and percent distribution. For comparison between two groups, the independent samples (t) test or Mann-Whitney tests were used. For comparison between categorical groups, the Chi square (X2) or Fisher's exact tests were used. Pearson correlation co-efficient (r-test) was used for correlating different variables. For all tests, P values < 0.04 were considered significant. For all tests, P values > 0.05 were considered insignificant.

Results

The study was a case control study conducted at Damietta General Hospital.It included 100 diabetic pregnant women during their third trimester (cases) and 100 women with normal pregnancy as control. Newborns with low 5-min Apgar score had higher plasticity index (P=0.052) than newborns with normal 5-min Apgar score. Regarding general characteristics, there was no significant difference between cases and control. The majority of diabetic mothers had gestational diabetes (40%) and had poor control of diabetes (25%).

Regarding ductus venosus Doppler assessment, there was no significant difference between cases and controls as regard all DV waves except the a-wave (P=0.023). Regarding DV ratios, we found that there was significant elevation of (S/D) (P=0.003 and 0.0011) among cases than controls. Regarding DV indices, we found that there was significant elevation of all DV indices among cases than controls including plasticity index (P=<0.011). Assessment of relation between Doppler assessment of ductus venosus indices and different variables revealed that poor control of diabetes was associated with elevated all DV indices among diabetic cases of the study. Also, pre-gestational DM was associated with significantly higher plasticity index (p=0.13) also, PVIV was elevated, but without significant difference (p=0.26). Newborns with low 5-min Apgar score had significantly higher plasticity index (p=0.02) than newborns with normal 5-min Apgar score; also, PVIV was elevated with low Apgar score, but without significant difference (p=0.10). There was significant positive correlation between DV-PI with both HbA1c and Apgar score. In contrast, there was no significant correlation between DV-PI with neither birth weight nor maternal age.

Table 1. Demographic characteristics of studied cases

Variables		Cases (n=100)	Control (n=100)	P
		Maternal		
Age (years)		32.3±4.7	28.9±5.13	0.25
BMI (kg/m^2)		34.6±10.5	29.04±9.2	0.013*
Parity	**Multiparous**	16 (11%)	11 (11%)	0.35
	Primiparous	24 (24%)	29 (35%)	
Gestational age (weeks)		29.4±2.7	30.3±3.07	0.17
Amniotic fluid index		16.31±6.25	14.43±4.7	<0.001*
Umbilical artery PI		1.24±0.32	1.18±0.24	0.21
		Neonatal		
Birth weight (g)		3546±814	3117±398	0.005*
Birth weight	**Appropriate for GA (AGA)**	26 (27%)	38 (40%)	0.001*
	Large for GA (LGA)	14 (21%)	2 (1%)	
5-min Apgar	**< 7**	6 (10%)	0 (0%)	0.020*
	≥ 7	34 (34%)	40 (40%)	

Table 2. Correlation between ductus venosus -plasticity index

Variable	DV-PI	
	r	P
Birth weight	0.02	0.15
Apgar score	0.13	0.005
Maternal age	0.11	0.203

Discussion

Diabetes is the most common metabolic disorder to affect pregnancy and is associated with increased maternal and neonatal morbidity (Sutton et al., 2017). Fetal cardiovascular development in women with diabetes mellitus can be affected by maternal hyperglycemia (Kulkarni et al., 2017). Ductus venosus blood flow plays an important role in right ventricular preload and hemodynamics (Chiu et al., 2016). Ductus venosus assessment is a crucial part of a prenatal fetal heart activity assessment; it is a valuable initial diagnostic and screening tool for many fetal cardiovascular abnormalities (Peixoto et al., 2016). Examination of ductus venosus

Doppler parameters among our cases resulted in variable figures between the simple waves and the more complex ratios and indices. Most of the studied parameters of our cases were within the normal reference ranges for DV flow velocities and waveform indices (Kessler et al., 2006 and Turan et al., 2014). These studies obtained their results from limited heterogeneous pregnancies; in addition, there is no local reference ranges for DV velocities. The choice of case control design aimed at eliminating the expected bias if a non-documented reference ranges was used. However, this design represented some limitation because of the inaccuracy in defining abnormal results. This study aimed to evaluate the parameters of ductus venosus Doppler ultrasound among diabetic pregnant women and its neonatal effect. Avcı et al. (2016) reported non-significant differences between fetuses with intracardiac echogenic focus and controls in the S-wave ($p = 0.01$) and D-wave ($p = 0.17$) velocities, and there was statistically significant differences between the groups in the v-descent ($p = 0.13$) and a-wave ($p = 0.14$) velocities.

In another cross-sectional study, a significant association between the presence of a-wave and heart related outflow tracts and right heart diseases was found ($P = 0.01$), no significant association of the S and D waves with other types of heart disease (Herrera et al., 2015). This change in the velocity of the v-descent and a-wave may be related to decreased end-systolic relaxation and increased atrial contraction. These changes in cardiac function may be related to restriction of AV valve motion owing to micro calcifications in the papillary muscles, leading to delayed atrial passive emptying, augmented atrial contraction, and a-wave depression; and restricted ventricular end-systolic relaxation owing to increased calcium deposition in the myocardium (Avcı et al., 2016).

On the other hand, Turan et al. (2011) demonstrated non-significant differences in UA-PI, DV-PIV and individual velocity ratios (S/v, S/D, S/a, v/D, v/a and D/a) between 63 cases with PGDM and controls during first-trimester screening at 11 to 14 weeks' gestation. Variation in timing of screening may be the corresponding cause . Also, Dahlback et al. (2016) suggested that the changes in the DV blood flow velocities during ventricular systole (S/ ES) were less frequent than alterations in ratios reflecting blood flows during atrial contraction in ventricular diastole (DV-PIV). Evaluation of multiple indices reflect the global cardiac function because semiquantitative DV Doppler indices, such as the PIV, give an incomplete reflection of cardiac function because relative changes in v- and D-wave velocities are not well reflected (Sanapo et al., 2014).

Our results are in consistent with several reports which evaluated cardiac performance in fetuses of diabetic mothers through their examination by fetal echocardiography, fetuses of poorly controlled diabetic mothers demonstrated significant differences in first-trimester diastolic myocardial function compared with non-diabetic controls (Turan et al., 2011). In a more recent study using two- dimensional speckle-tracking echocardiography, unfavorable changes occurred in the fetal myocardium in response to both maternal DM (Kulkarni et al., 2017). In summary, results of the present study highlighted the possible fetal cardiac effects of maternal diabetes mellitus and proved the effect of poor control of diabetes on the DV Doppler indices. However, these studies need to be further validated.

Conclusion

Diabetic pregnancies demonstrated significant difference of ductus venosus Doppler parameters compared with non-diabetic controls, possibly indicating a fetal cardiac effect.

Recommendation

It may be useful to include DV-Doppler indices in the antenatal management of pregnancies complicated by diabetes mellitus. Proper antenatal management of diabetic. Further studies are recommended on large scale to confirm these results, as well as special focusing on variable aspects of diabetic complication such as intra-uterine growth restriction and congenital anomalies.

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