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Role of Fetal Echocardiography in the Evaluation of Fetal Heart in Diabetic Pregnancies

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Abstract

Maternal DM is usually associated with structural and functional changes in the fetal heart. Fetal echocardiography plays a key role in the identification of these changes. The aim of this paper assesses the importance of fetal echocardiography in the detection of structural and functional diseases of the heart in diabetic pregnant mothers' fetuses and compare them with uncomplicated pregnancy. We enrolled 100 pregnant mothers with age between 18 and 45 years and the age of mean is about 27.68 ± 3.11,50 diabetic pregnant women and 50 non-diabetic pregnant women; the diabetic group subdivided into; pre-GDM: 15 patients & GDM: 35 patients. Fetal echocardiography was done for all cases. We evaluate RV & LV dimensions and function by conventional M mode, 2D and Doppler imaging. Our study shows significant difference in comparing cases with control group as regards PWDd, PWDs, but highly statistically significant difference as regard IVSd, IVSs, EF%, Left atrial diameter, Aortic to LA diameter ratio, RV diameter and Stroke volume (SV).This means higher risk if LVH (HCM) in fetuses of diabetic mothers, While there was no difference significantly between them as regard LVESD, LVEDD, Aortic diameter, RV/LVED. Also, it shows a statistically significant difference between Pregestational and gestaional group regarding LVESD, RV, TVEV, TVAV and TV max V, AV max V, PV mean V dimensions and highly statistically significant difference regarding LVEDD, TV maxV, in contrast, there was no difference among the studies groups as regard IVSd, IVSs, PWDd, PWDs, AO, LA, LA/AO, RV/L ED ratio, EF (%), MVEV, MVAV, MV E/A ratio, MV max V, MV mean V, TV E/A ratio, TV mean V, AV mean V, PV max v<SV, (MPI) Tie index with p-value > 0.05. A higher incidence of congenital structural as well as functional abnormalities in fetal hearts is seen within fetuses of diabetic pregnant mothers. Fetal echocardiography is a sensitive parameter in the detection of these abnormalities.

Keywords: Structural and functional heart disease, Maternal diabetes mellitus, Fetal echocardiography.

1. Introduction

Maternal DM is considered to be the most common metabolic disorder complicating pregnancy. DM during pregnancy can be classified into type I, type II, and gestational diabetes [1]. WHO states that heart defects represent about 42 % of infant mortality, affecting their future development [2]. The incidence of detected anomalies is five times more in diabetic mother's fetuses [3]. Fetal echocardiography has shown progress in the near-past years for being a sensitive screening tool with its characteristics of availability and non-invasiveness used as an early prediction of CHD [4]. The major component of fetal heart assessment is to assess systolic and diastolic functions, with more appreciation given to diastolic function evaluation as a prognostic predictor of fetal cardiomyopathies [5]. Spectral pulsed Doppler echocardiography provides a safe accurate tool in the assessment of diastolic function, as via detection of the atrioventricular valve's velocities, the volume of the ventricular filling during diastole can be assessed and then, the state of ventricular muscles and their compliance to relax [6].

2. Patients and Methods

Our study was a prospective study of case-control type and was conducted over 100 pregnant mothers aged 18-45 years with a mean age of 27.68 ± 3.11 and separated into two types of population; group one, recruited from 50 pregnant mothers diagnosed to have diabetes mellitus with its two types; gestational and pre-gestational one, and group two included 50 pregnant mothers with normal pregnancies. The study was conducted at the clinic of Radiodiagnosis as well as Obstetrics and Gynecology Departments of Alzahraa University Hospital, as long as the period between October 2021 and September 2023. Approval of the protocol of this study has been done by the research committee of ethics at Alazhar University Hospital. Then, written consents from the patients were collected after being informed of the detailed methodology. The objective of this study is to delineate the role of fetal echocardiography in the evaluation of fetal heart in diabetic pregnancies by using Doppler echocardiography.

2.1 Eligibility criteria

Patients with gestational age ranging from 18-30 weeks in pregnant women suffering from either gestational or pre-gestational diabetes, and normal uncomplicated singleton pregnancy were included in the study. The study also included pregnant women with suspected increased risk of being of more advanced age, more than 35 years, with associated history of diabetes mellitus running in the family, past history of diabetes during the past gestations, macrosomic baby and neonatal death soon after birth. All participants recruited in this research were asked about their personal and obstetric history, clinicolaboratory investigations with special emphasis on blood glucose level, and fetal echocardiographic examination.

2.2 Exclusion criteria

The exclusion criteria were pregnant women with any heart disease whatever the etiology, maternal hypertension, preeclampsia, pregnant women with marked obesity, pregnant women with other metabolic diseases: kidney diseases, hepatic diseases and phenyl-ketonuria, twin pregnancies, pregnancies associated with placental insufficiency, and exposure to teratogens.

2.3 Imaging protocol

All necessary routine fetal non-cardiac measures were taken as well as routine fetal cardiac measures. A full sequential analysis of fetal echo-cardiography was done and echocardiographic views necessary to perform a complete evaluation of the fetal cardiac system were obtained.

2.4 Two-dimensional (2D)

The normal anatomical landmarks of fetal cardiac chambers and their relations to each

other and the major outflow tracts, the AV valves, inter-atrial and inter-ventricular septae, sagittal view of the descending aorta were sequentially assessed in a systematic order.

2.5 M-mode

Measurement of the end-diastolic (LVEDD) and end-systolic (LVESD) dimension of left ventricle to assess fractional shortening (FS) and interventricular septal thickness during diastole (IVSs, IVSd), posterior free wall of left ventricle (LVPWD), Left atrial (LA) and aortic root (AO) dimension, was done in subcostal view of 4-chamber via setting the cursor perpendicular to the septum between both ventricles.

2.6 Conventional Doppler Echocardiography

Doppler waveform for the left myocardial performance index (MPI= Tiw index) was done, by placing the sample volume distal to the mitral valve and proximal to the aortic valve in the 4-chamber view to obtain an assessment of both inflow and outflow waveform simultaneously form the left ventricle. We calculate the time intervals (Iso-volumic contraction time (ICT) from mitral valve closure click to aortic valve opening click), (Iso-volumic relaxation time (IRT) from aortic valve closure click to mitral valve opening click), and (Ejection time (ET) from opening to closure of aortic valve. So, the Tie index 'MPI' is calculated as (ICT+IRT/ET).

Then, Blood inflow across both mitral and tricuspid valves was calculated via using spectral Doppler within the ventricles just distal to A-V valves. E and A velocities of each A-V valve were measured, and then, the ratio between them E/A ratio was calculated. Color and pulsed wave Doppler on aortic, pulmonary and ductus flow, were obtained with aortic, pulmonary maximum and mean velocities were obtained and the continuous flow of ductus during diastole was assured to emphasis that ductus maximum velocity was higher than aortic and pulmonary maximum velocities, denoting low placental vasculature resistance.

2.7 Statistical Analysis

Ultrasound equipment used was 3.5- 5-MHz transabdominal at the ultrasound unit of the Obstetrics and Gynecology department at Al-Azhar University Hospitals in Egypt. All females were evaluated for Gross anatomical defects, foetal viability, and foetal biometry [biparietal diameter - femur length - abdominal circumference] were evaluated using transabdominal ultrasound.

3. Results

From 100 studied pregnant mothers, our population were classified into two groups, group one, the case group, was recruited from 50 diabetic women and group two, the control group, included 50 healthy non-diabetic pregnant women, when comparing both groups as regards maternal characteristics, we found that both groups are similar except for gravidity being much higher in cases rather than control (Table. 1. We found that among the 50 diabetic pregnant women about 19 patients are of good glycemic control and about 31 patients are of poor glycemic control Figure. 1, Table. 2. We found that the mean thickness of interventricular septum in diabetic mothers was 0.47 ± 0.14 cm and 0.37 ± 0.13 cm in healthy non-diabetic mothers, denoting a high difference between cases and control as regards IVSd, IVSs, LA/AO and EF with P-value < 0.01, being more increased in cases in comparison to the control group Figure.2, Table .3. We found a high statistically significant difference among the studied population regarding MV E/A Ratio and MVEV being lower in cases than in the control group, denoting impaired diastolic function in diabetic cases (Figure. 3, Table 4). We found a highly significant difference among both groups as regards SV and Tie index with P-value < 0.01, being decreased

SV in cases in comparison to the control group and increased Tie index in the cases group with the mean tie index value in diabetic mothers was 0.51 ± 0.11, denoting impairment of global cardiac function Figure. 4, Table .5.

Table (1): Comparison of the two studied categories regarding the demographic data.

		Control group No. = 50	Cases group No. = 50	Test value	P-value	Sig.
Maternal age	Mean ± SD	27.68 ± 3.11	28.66 ± 4.01	-1.364•	0.176	NS
	Range	20 – 33	23 – 40			
Gravidity	**Median (IQR)**	**1 (1-2)**	**2 (1-3)**	**-2.673‡**	**0.008**	**HS**
	Range	**1 – 4**	**1 – 6**			
GA	Mean ± SD	25.58 ± 1.67	25.68 ± 1.36	-0.328•	0.743	NS
	Range	24 – 28	24 – 28			
BMI	Mean ± SD	24.82 ± 3.10	24.71 ± 3.54	0.168•	0.867	NS
	Range	19 – 29	19 – 33.7			

Table (2): Diabetic control among the studied cases.

		Cases group No. = 50 (%)
HbA1C	**Mean ± SD**	**7.90 ± 1.17**
	Range	**6.6 – 12**
HA1C.C	**Good**	**19 (38.0%)**
	Poor C	**31 (62.0%)**

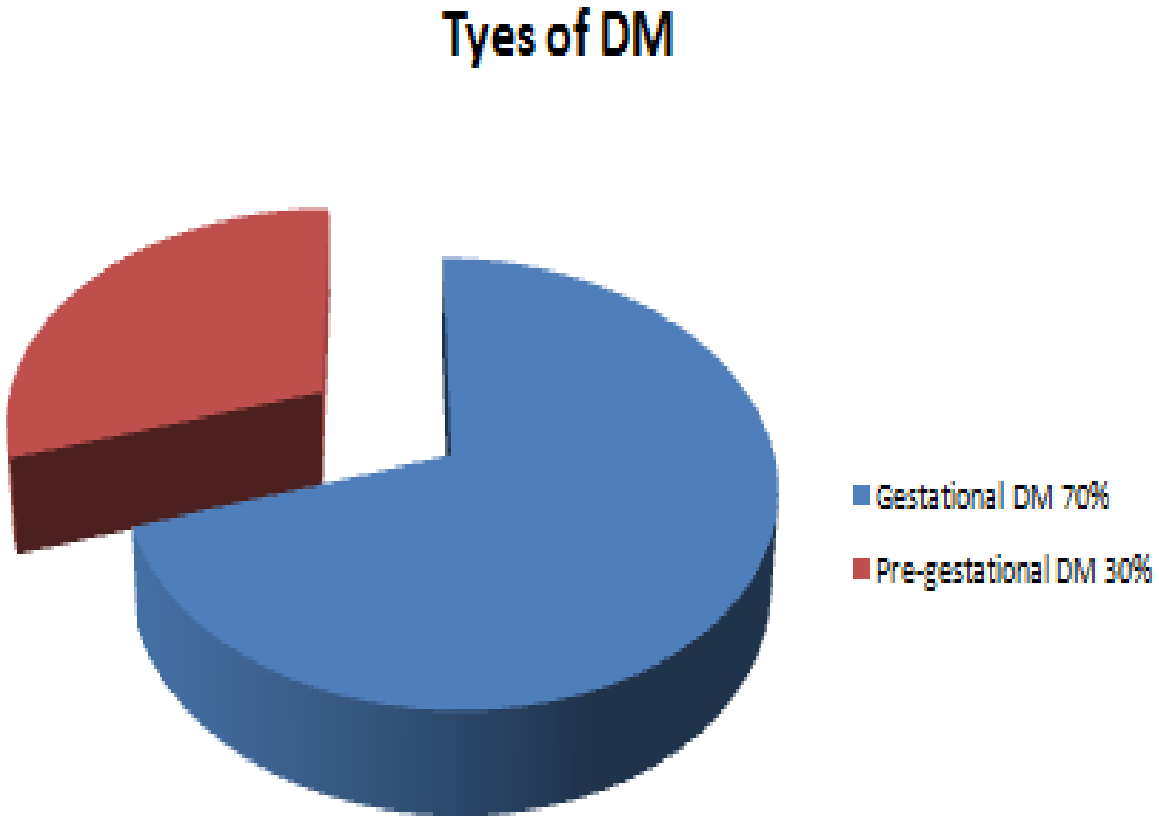

Figure (1): Fetal ultrasonographic biometry in both studied groups.

Table (3): Comparison among the two studied population categories regarding fetal echocardiographic geometric data.

		Control group No. = 50	Cases group No. = 50	Test value•	P-value	Sig.
LVEDD	Mean ± SD	0.98 ± 0.16	1.02 ± 0.24	-0.973	0.333	NS
	Range	0.67 − 1.28	0.6 − 1.6			
LVESD	Mean ± SD	0.56 ± 0.10	0.61 ± 0.16	-1.846	0.068	NS
	Range	0.39 − 0.7	0.3 − 0.9			
IVS diastole	**Mean ± SD**	**0.37 ± 0.13**	**0.47 ± 0.14**	**-4.081**	**0.000**	**HS**
	Range	**0.2 − 0.63**	**0.2 − 0.7**			
LVPWDd	**Mean ± SD**	**0.37 ± 0.09**	**0.43 ± 0.12**	**-2.549**	**0.012**	**S**
	Range	**0.2 − 0.56**	**0.2 − 0.6**			
LVPWDs	**Mean ± SD**	**0.41 ± 0.10**	**0.46 ± 0.13**	**-2.193**	**0.031**	**S**
	Range	**0.16 − 0.62**	**0.2 − 0.7**			
AO	Mean ± SD	0.64 ± 0.14	0.69 ± 0.14	-1.505	0.135	NS
	Range	0.42 − 1	0.45 − 1.2			
RV	**Mean ± SD**	**0.76 ± 0.18**	**1.17 ± 0.27**	**-8.957**	**0.000**	**HS**
	Range	**0.44 − 1.08**	**0.6 − 1.7**			
RV/LD ED	Mean ± SD	1.11 ± 0.06	1.13 ± 0.22	-0.599	0.551	NS
	Range	1 − 1.22	0.13 − 1.75			
IVSs	**Mean ± SD**	**0.43 ± 0.11**	**0.61 ± 0.37**	**-3.417**	**0.001**	**HS**
	Range	**0.25 − 0.7**	**0.3 − 3**			
LA	**Mean ± SD**	**0.54 ± 0.10**	**0.85 ± 0.20**	**-9.768**	**0.000**	**HS**
	Range	**0.35 − 0.71**	**0.5 − 1.24**			
LA.AO	**Mean ± SD**	**0.85 ± 0.12**	**1.24 ± 0.22**	**-11.197**	**0.000**	**HS**
	Range	**1 − 1**	**1 – 2**			
EF	**Mean ± SD**	**80.49 ± 5.67**	**77.16 ± 5.54**	**2.967**	**0.004**	**HS**
	Range	**67 − 92**	**67 – 88**			

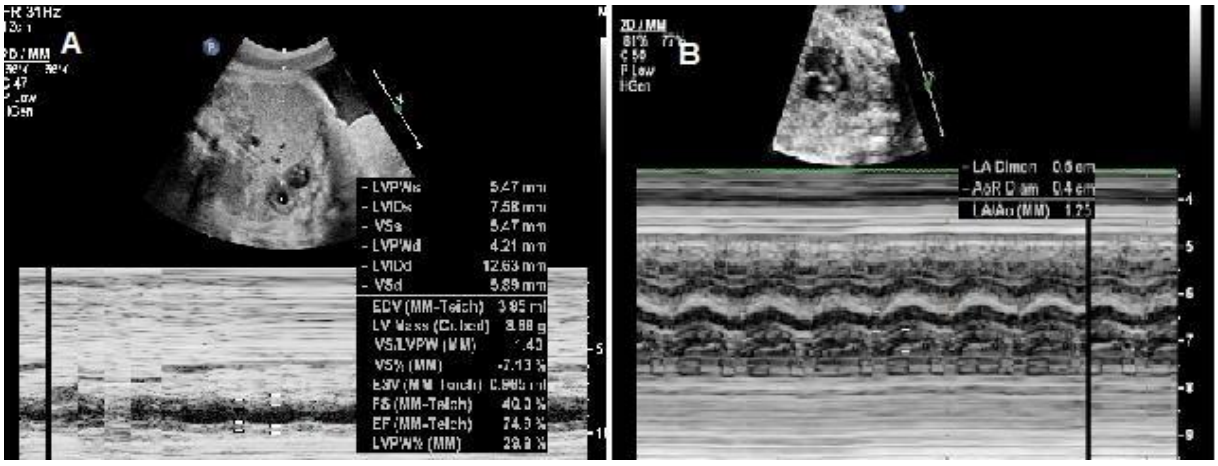

Figure (2): Fetal ultrasonographic biometry in both studied groups.

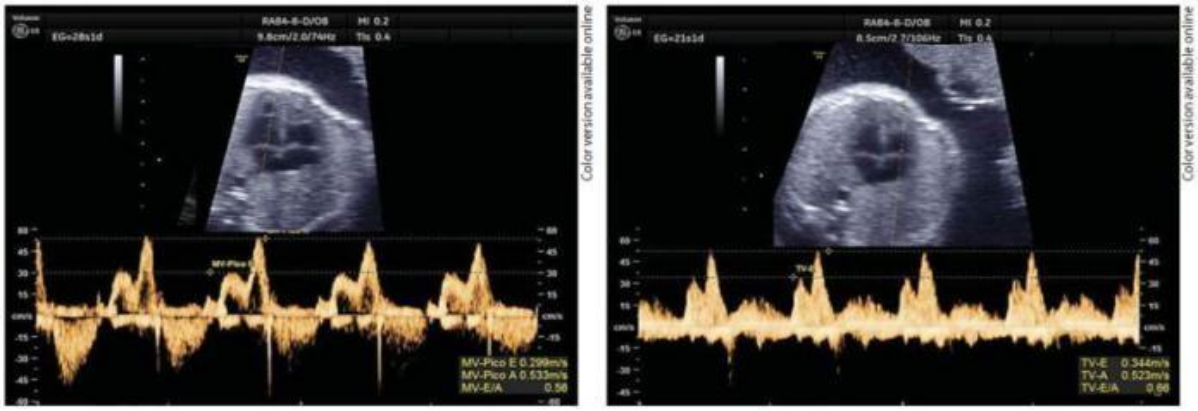

Figure (3): Mitral E/A waveform, Tricuspid E/A waveform.

Table (4): Comparison among the two studied categories of population regarding Doppler assessment.

		Control group No. = 50	Cases group No. = 50	Test value	P-value	Sig.
MVEV	**Mean ± SD**	**0.29 ± 0.06**	**0.26 ± 0.04**	**0.101**	**0.012**	**S**
	Range	**0.21 − 0.43**	**0.19− 0.41**			
MVAV	Mean ± SD	0.47 ± 0.08	0.46 ± 0.10	0.671	0.504	NS
	Range	0.31 − 0.64	0.3 − 0.7			
MVE|A ratio	**Mean ± SD**	**0.65± 0.11**	**0.60 ± 0.08**	**-2.723**	**0.008**	**HS**
	Range	**0.45 – 1**	**0.42– 0.73**			
MV max V	Mean ± SD	0.51 ± 0.09	0.54 ± 0.12	-1.768	0.080	NS
	Range	0.33 − 0.67	0.36 − 0.9			
MV mean V	Mean ± SD	0.31 ± 0.08	0.31 ± 0.06	-0.245	0.807	NS
	Range	0.18 − 0.44	0.23 − 0.47			
TVEV	Mean ± SD	0.31 ± 0.04	0.31 ± 0.06	-0.200	0.842	NS
	Range	0.23 − 0.41	0.21 − 0.41			
TVAV	Mean ± SD	0.49 ± 0.06	0.50 ± 0.11	-0.308	0.759	NS
	Range	0.4 − 0.63	0.28 − 0.79			
TVE\A ratio	Mean ± SD	0.60 ± 0.11	0.63 ± 0.11	-1.417	0.160	NS
	Range	0.36 − 0.76	0.43 – 1			
TV maX V	Mean ± SD	0.53 ± 0.13	0.54 ± 0.11	-0.277	0.782	NS
	Range	0.36 − 0.81	0.36 − 0.83			
TV mean V	Mean ± SD	0.32 ± 0.08	0.31 ± 0.07	0.690	0.492	NS
	Range	0.2 − 0.48	0.18 − 0.48			
AVmaxV	Mean ± SD	0.78 ± 0.15	0.75 ± 0.21	0.595	0.553	NS
	Range	0.59 − 1.2	0.3 − 1.3			
AV mean V	Mean ± SD	0.51 ± 0.08	0.50 ± 0.15	0.632	0.529	NS
	Range	0.37 − 0.73	0.16 − 0.79			
PV maxV	Mean ± SD	0.81 ± 0.12	0.79 ± 0.26	0.450	0.654	NS
	Range	0.62 – 1	0.39 − 1.93			
PV mean V	Mean ± SD	0.52 ± 0.07	0.51 ± 0.17	0.105	0.916	NS
	Range	0.36 − 0.61	0.21 − 1.12			
PDA flow	Mean ± SD	1.07 ± 0.17	1.01 ± 0.16	1.918	0.058	NS
	Range	0.71 − 1.3	0.5 − 1.3			

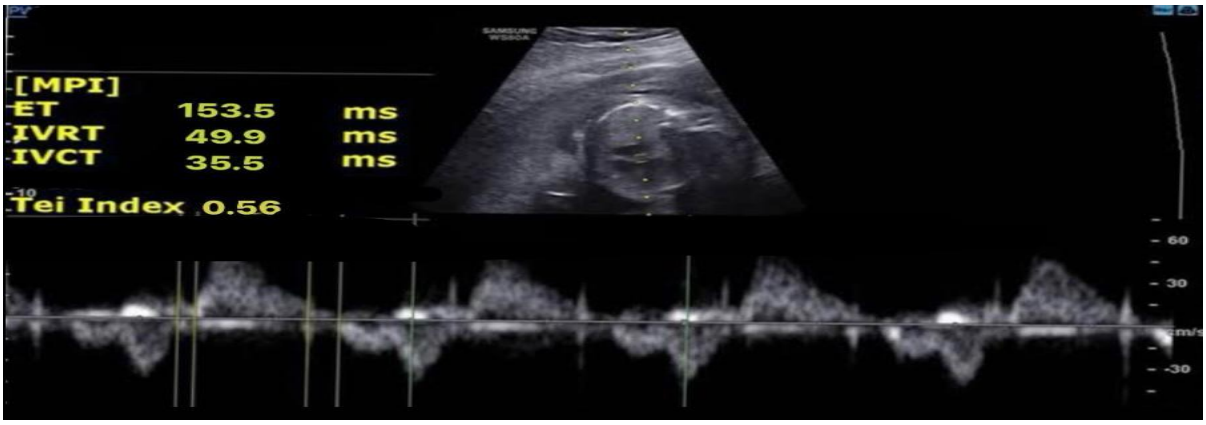

Figure (4): Spectral Doppler of MPI assessment with impaired global cardiac function.

Table (5): Comparison among the two studied categories of population as regards Stroke volume (SV) and Myocardial performance index (MPI= Tie index).

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		Control group No. = 50	Cases group No. = 50	Test value•	P-value	Sig.
SV	**Mean ± SD**	**1.92 ± 0.75**	**1.40 ± 0.93**	**3.069**	**0.003**	**HS**
	Range	**0.28 – 3**	**0.19 – 5**			
	Range	60 – 80	60 – 80			
Tie index	**Mean ± SD**	**0.38 ± 0.02**	**0.51 ± 0.11**	**-7.752**	**0.000**	**HS**
	Range	**0.35 − 0.42**	**0.38 − 0.72**			

We found that a high difference was signified as regards LVEDD being more decreased in pre-gestational diabetic pregnant women than gestational ones (Figure .5, Table. 6). We found that a high difference was signified among gestational as well as pre-gestational diabetic mothers as regards TV max V being more increased in gestational group in comparison to pre-gestational one, and there was statistically significance between TVEV, TVAV, TV max V and PV mean V, AV max V., and the rest of other parameters were insignificant (Table 7). We found that a high difference was signified among properly as well as poorly controlled groups as regards LVEDD, LVESD, IVSd, PWDd, PWDs, RV, LA, EF. with p-value < 0.01, being increased in poor glycemic control in comparison to good, controlled ones, while EF being decreased in poor glycemic control group in comparison to good, controlled ones. And the rest of the other parameters were insignificant (Table 8). We found that a high difference was signified among properly as well as poorly controlled groups as regards TV max V P-value< 0.01, being more increased in a poor controlled group than good controlled one, while the rest of the other parameters were insignificant (Table: 9). We found that a high difference was signified among good and poor control of diabetes mellitus as regarding Tie index, being high in poor control patients, with no difference as regards SV (Table 10). One of our cases appeared to have a structural heart defect known as transposition of great arteries with associated VSD manifested by the abnormal orientation of great vessels of the fetal heart when emerging from the ventricles, as aorta arising from RV and PA arising from LV with associated VSD And abnormal 3 vessel view that showed only 2 vessels instead of 3, AO and SVC, while the pulmonary artery arising more caudally (Figure .4), and the other was diagnosed to have tetralogy of Fallot manifested by overriding aorta arising from both ventricles with VSD and pulmonary stenosis (Figure .4).

Table (6): Comparison between the two types of diabetic group regarding fetal echo geometric data.

		Pre gestational No. = 15	Gestational No. = 35	Test value•	P-value	Sig.
LVEDD	Mean ± SD	0.87 ± 0.18	1.09 ± 0.23	**-3.206**	**0.002**	**HS**
	Range	0.7 − 1.4	0.6 − 1.6			
LVESD	Mean ± SD	0.53 ± 0.13	0.64 ± 0.16	**-2.377**	**0.021**	**S**
	Range	0.4 − 0.9	0.3 − 0.9			
IVS diastole	Mean ± SD	0.42 ± 0.15	0.50 ± 0.12	-1.898	0.064	NS
	Range	0.2 − 0.6	0.3 − 0.7			
PWDd	Mean ± SD	0.41 ± 0.13	0.43 ± 0.11	-0.466	0.644	NS
	Range	0.2 − 0.6	0.27 − 0.6			
PWDs	Mean ± SD	0.42 ± 0.14	0.48 ± 0.12	-1.454	0.152	NS
	Range	0.2 − 0.62	0.3 − 0.7			
AO	Mean ± SD	0.69 ± 0.10	0.69 ± 0.15	0.029	0.977	NS
	Range	0.5 − 0.8	0.45 − 1.2			
RV	Mean ± SD	1.05 ± 0.24	1.22 ± 0.27	**-2.115**	**0.040**	**S**
	Range	0.7 − 1.5	0.6 − 1.7			
RV/LD ED	Mean ± SD	1.15 ± 0.36	1.12 ± 0.13	0.341	0.735	NS
	Range	0.13 − 1.75	1 − 1.6			
IVSs	Mean ± SD	0.69 ± 0.66	0.58 ± 0.12	0.986	0.329	NS
	Range	0.3 – 3	0.33 − 0.8			
LA	Mean ± SD	0.84 ± 0.15	0.85 ± 0.22	-0.258	0.798	NS
	Range	0.5 – 1	0.6 − 1.24			
LA.AO	Mean ± SD	1.21 ± 0.13	1.26 ± 0.25	-0.639	0.526	NS
	Range	1 − 1.43	0.97 − 1.8			
EF	Mean ± SD	77.73 ± 4.43	76.91 ± 6.00	0.475	0.637	NS
	Range	71 – 85	67 – 88			

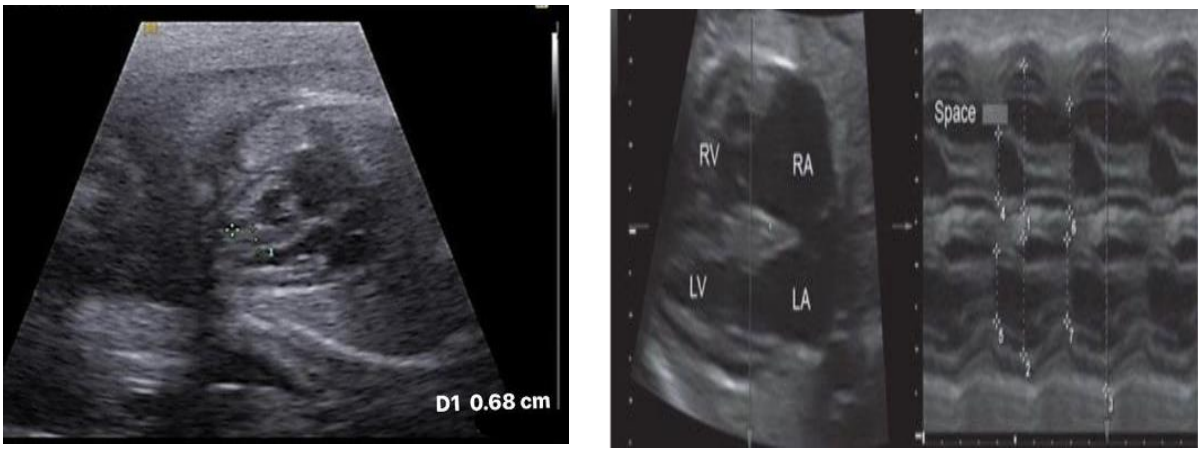

Figure (5): 2D and M-mode US for measurement of ventricular geometry of a case of pre-gestational diabetes.

Table (7): Comparison between the two types of diabetic groups regarding Doppler assessment.

		Pre gestational No. = 15	Gestational No. = 35	Test value•	P-value	Sig.
MVEV	Mean ± SD	0.27 ± 0.08	0.30 ± 0.05	-1.269	0.211	NS
	Range	0.2 – 0.45	0.21 – 0.48			
MVAV	Mean ± SD	0.44 ± 0.11	0.47 ± 0.10	-0.906	0.370	NS
	Range	0.31 – 0.63	0.3 – 0.7			
MVE|A ratio	Mean ± SD	0.63 ± 0.10	0.66 ± 0.11	-0.909	0.368	NS
	Range	0.45 – 0.77	0.48 – 1			
MV max V	Mean ± SD	0.59 ± 0.14	0.52 ± 0.11	1.713	0.093	NS
	Range	0.43 – 0.9	0.36 – 0.78			
MV mean V	Mean ± SD	0.32 ± 0.07	0.31 ± 0.06	0.603	0.549	NS
	Range	0.24 – 0.47	0.23 – 0.45			
TVEV	**Mean ± SD**	**0.28 ± 0.05**	**0.32 ± 0.06**	**-2.152**	**0.036**	**S**
	Range	**0.21 – 0.39**	**0.23 – 0.41**			
TVAV	**Mean ± SD**	**0.45 ± 0.11**	**0.52 ± 0.11**	**-2.216**	**0.031**	**S**
	Range	**0.28 – 0.65**	**0.32 – 0.79**			
TVE\A ratio	Mean ± SD	0.65 ± 0.11	0.62 ± 0.11	0.655	0.516	NS
	Range	0.47 – 0.79	0.43 – 1			
TV max V	**Mean ± SD**	**0.48 ± 0.06**	**0.57 ± 0.12**	**-2.742**	**0.009**	**HS**
	Range	**0.39 – 0.59**	**0.36 – 0.83**			
TV mean V	Mean ± SD	0.29 ± 0.06	0.32 ± 0.07	-1.285	0.205	NS
	Range	0.18 – 0.42	0.2 – 0.48			
AV maxV	**Mean ± SD**	**0.65 ± 0.23**	**0.80 ± 0.19**	**-2.356**	**0.023**	**S**
	Range	**0.3 – 1.3**	**0.33 – 1.1**			
AV mean V	Mean ± SD	0.44 ± 0.14	0.52 ± 0.14	-1.973	0.054	NS
	Range	0.18 – 0.76	0.16 – 0.79			
PV maxV	Mean ± SD	0.69 ± 0.16	0.83 ± 0.28	-1.823	0.075	NS
	Range	0.39 – 0.94	0.48 – 1.93			
PV mean V	**Mean ± SD**	**0.44 ± 0.13**	**0.55 ± 0.18**	**-2.129**	**0.038**	**S**
	Range	**0.21 – 0.61**	**0.23 – 1.12**			
PDA flow	Mean ± SD	1.01 ± 0.11	1.01 ± 0.18	-0.002	0.999	NS
	Range	0.8 – 1.1	0.5 – 1.3			
	Range	0.18 – 0.42	0.2 – 0.48			

Table (8): Comparison between both groups regarding the relation of HbA1c level with ECHO data.

		Good HbA1c C No. = 19 (mm)	Poor HbA1c C No. = 31(mm)	Test value•	P-value	Sig.
LVEDD	**Mean ± SD**	**0.87 ± 0.23**	**1.11 ± 0.20**	**-3.783**	**0.000**	**HS**
	Range	**0.6 − 1.4**	**0.8 − 1.6**			
LVESD	**Mean ± SD**	**0.49 ± 0.14**	**0.68 ± 0.12**	**-4.946**	**0.000**	**HS**
	Range	**0.3 − 0.8**	**0.5 − 0.9**			
IVS diastole	**Mean ± SD**	**0.36 ± 0.09**	**0.55 ± 0.11**	**-6.617**	**0.000**	**HS**
	Range	**0.2 − 0.5**	**0.3 − 0.7**			
PWDd	**Mean ± SD**	**0.32 ± 0.06**	**0.49 ± 0.10**	**-6.370**	**0.000**	**HS**
	Range	**0.2 − 0.43**	**0.3 − 0.6**			
PWDs	**Mean ± SD**	**0.37 ± 0.08**	**0.52 ± 0.11**	**-4.881**	**0.000**	**HS**
	Range	**0.2 − 0.5**	**0.34 − 0.7**			
AO	Mean ± SD	0.63 ± 0.10	0.72 ± 0.15	-2.158	0.036	NS
	Range	0.45 − 0.8	0.5 − 1.2			
RV	**Mean ± SD**	**1.00 ± 0.30**	**1.27 ± 0.19**	**-3.855**	**0.000**	**HS**
	Range	**0.6 − 1.6**	**0.9 − 1.7**			
RV/LD ED	Mean ± SD	1.09 ± 0.27	1.16 ± 0.18	-1.125	0.266	NS
	Range	0.13 − 1.6	1 − 1.75			
IVSs	Mean ± SD	0.60 ± 0.60	0.62 ± 0.11	-0.217	0.829	NS
	Range	0.3 – 3	0.4 − 0.8			
LA	**Mean ± SD**	**0.74 ± 0.16**	**0.92 ± 0.19**	**-3.403**	**0.001**	**HS**
	Range	**0.5 – 1**	**0.63 − 1.24**			
LA.AO	Mean ± SD	1.17 ± 0.18	1.29 ± 0.22	-2.063	0.045	NS
	Range	0.97 − 1.5	1 − 1.8			
EF	**Mean ± SD**	**79.95 ± 5.58**	**75.45 ± 4.85**	**3.004**	**0.004**	**HS**
	Range	**70 – 88**	**67 – 87**			

Table (9): Relation of HbA1c with ECHO Doppler assessment.

		Good HbA1c C No. = 19	Poor HbA1c C No. = 31	Test value•	P-value	Sig.
MVEV	Mean ± SD	0.28 ± 0.07	0.29 ± 0.06	-0.758	0.452	NS
	Range	0.21 − 0.48	0.2 − 0.45			
MVAV	Mean ± SD	0.45 ± 0.11	0.46 ± 0.10	-0.217	0.829	NS
	Range	0.31 − 0.7	0.3 − 0.67			
MVE|A ratio	Mean ± SD	0.63 ± 0.09	0.66 ± 0.12	-0.994	0.325	NS
	Range	0.45 − 0.77	0.48 − 1			
MV max V	Mean ± SD	0.58 ± 0.14	0.52 ± 0.10	1.848	0.071	NS
	Range	0.36 − 0.9	0.36 − 0.78			
MV mean V	Mean ± SD	0.32 ± 0.07	0.31 ± 0.06	0.571	0.570	NS
	Range	0.23 − 0.47	0.23 − 0.45			
TVEV	Mean ± SD	0.31 ± 0.06	0.31 ± 0.06	0.504	0.616	NS
	Range	0.24 − 0.41	0.21 − 0.41			
TVAV	Mean ± SD	0.51 ± 0.10	0.50 ± 0.12	0.284	0.777	NS
	Range	0.32 − 0.65	0.28 − 0.79			
TVE\A ratio	Mean ± SD	0.63 ± 0.09	0.63 ± 0.12	-0.128	0.898	NS
	Range	0.47 − 0.79	0.43 – 1			
TV max V	**Mean ± SD**	**0.48 ± 0.10**	**0.58 ± 0.11**	**-3.289**	**0.002**	**HS**
	Range	**0.36 − 0.65**	**0.43 − 0.83**			
TV mean V	Mean ± SD	0.30 ± 0.08	0.32 ± 0.06	-0.817	0.418	NS
	Range	0.18 − 0.42	0.22 − 0.48			
AV maxV	Mean ± SD	0.77 ± 0.24	0.74 ± 0.20	0.361	0.720	NS
	Range	0.37 − 1.3	0.3 − 1.1			
AV mean V	Mean ± SD	0.48 ± 0.16	0.51 ± 0.14	-0.708	0.483	NS
	Range	0.18 − 0.76	0.16 − 0.79			
PV maxV	Mean ± SD	0.80 ± 0.21	0.78 ± 0.28	0.342	0.734	NS
	Range	0.39 − 1.1	0.44 − 1.93			
PV mean V	Mean ± SD	0.52 ± 0.16	0.51 ± 0.18	0.223	0.824	NS
	Range	0.21 − 0.76	0.21 − 1.12			
PDA flow	Mean ± SD	0.99 ± 0.16	1.01 ± 0.17	-0.498	0.620	NS
	Range	0.7 − 1.2	0.5 − 1.3			

Table (10): Relation of HbA1c level with SV and Tie index.

		Good HbA1c C	Poor HbA1c C	Test value	P-value	Sig.
		No. = 19	No. = 31			
SV	Mean ± SD	1.34 ± 0.72	1.43 ± 1.05	-0.342	0.734	NS
	Range	0.69 – 3	0.19 – 5			
Tie index	**Mean ± SD**	**0.41 ± 0.02**	**0.57 ± 0.10**	**-6.971**	**0.000**	**HS**
	Range	**0.38 – 0.45**	**0.38 – 0.72**			

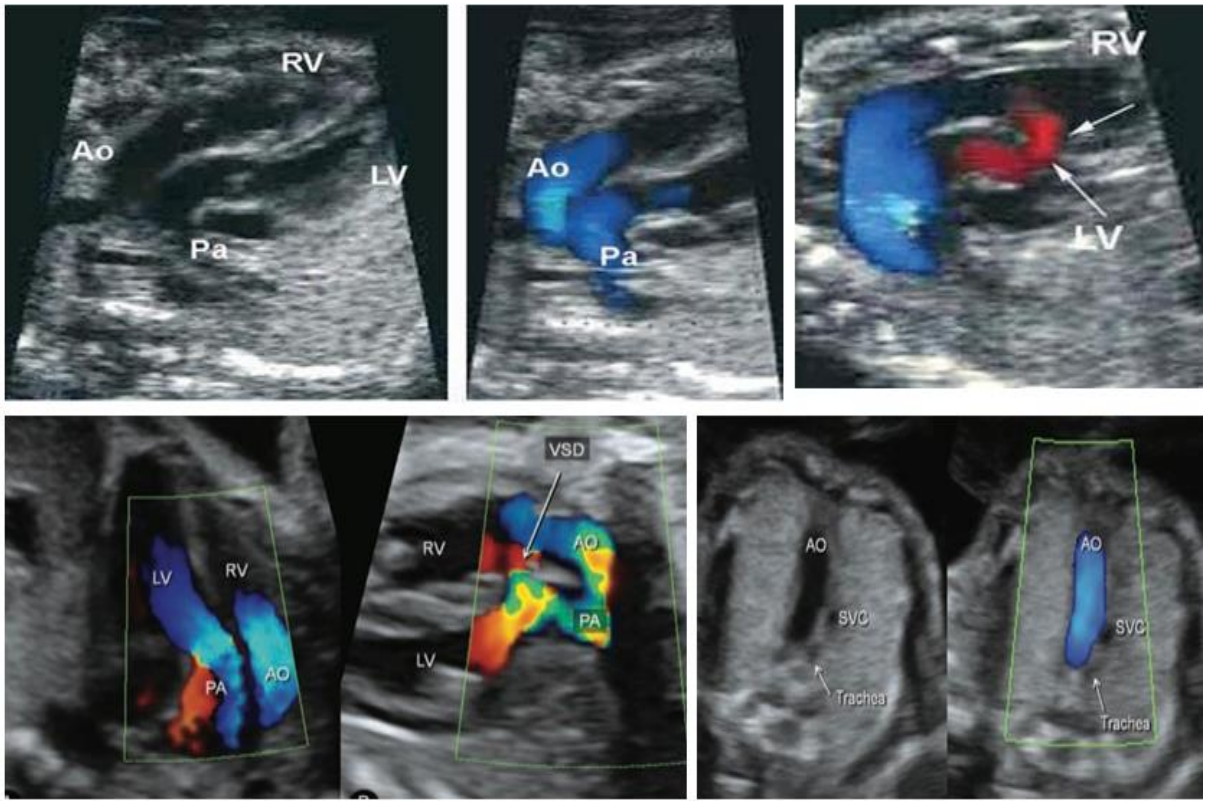

Figure (6): 2D US (a) with Color Doppler ultrasound (b,c) of a case of TGA with VSD.

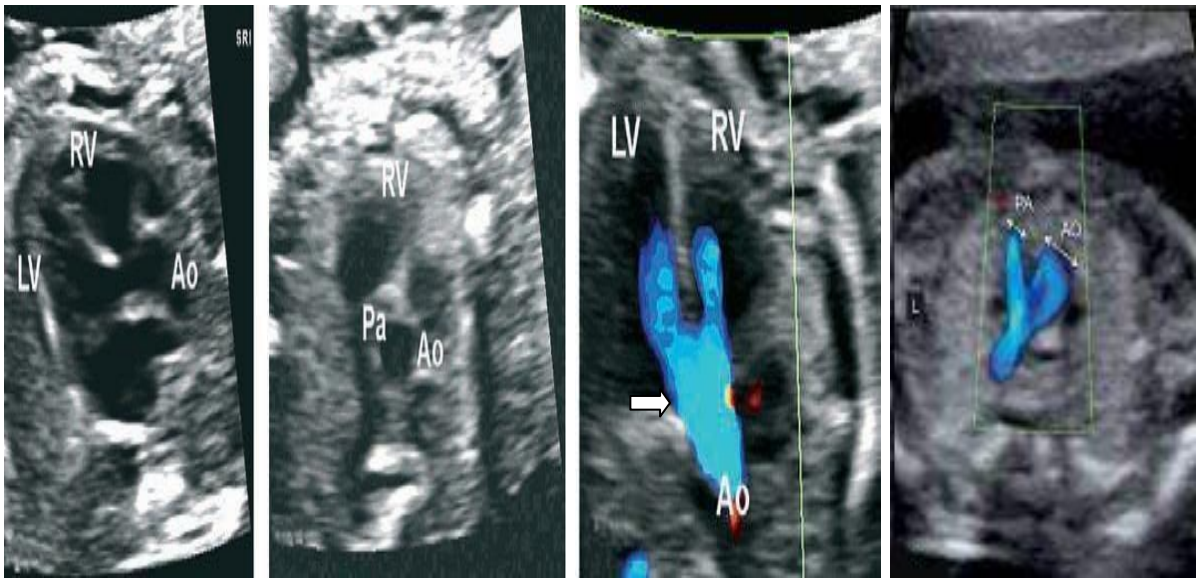

Figure (7): 2D ultrasound and colour Doppler US of a case of tetralogy of Fallout.

4. Discussion

Our study was aiming to delineate the role of fetal echocardiography in evaluating the impact of DM during pregnancy on fetal heart structure as well as function.

Furthermore, to compare the effect of GDM and pre-GDM on fetal heart and the relation between maternal glycemic control and these changes in comparison to normal one. The current study included 100 pregnant women, fifty diabetic (either gestational or pregestational DM) and fifty healthy non-diabetic age-matched pregnant women as a control group. The mean maternal age was 28.66 ± 4 in the cases group, while in the control group, it was 27.68 ± 3.11, fetal echocardiography was performed within a comparable gestational age of 25.68 ± 1.36weeks in the cases group and at 25.58 ± 1.67weeks in the control group and illustrated that no significant relation among both studied population categories as regards age of pregnant mothers or gestational age with p value **<**0.00.

As regard risk factors, in our study **regarding BMI**, no difference was signified among studied population categories with estimated p-value >0.05, but a high difference was signified among case and control group as regarding **gravidity** with estimated p value **<**0.01, as illustrated in Table (1).

This is a similarity with **Rahman et al. [7]** study in which both groups were similar with regard to maternal age (25.9 ±3.5 years in diabetic group and 25.2 ± 3.2 years in control group, p=0.130).

In disagreement with **El khouly et al. [8] study,** a difference was noted regarding the gestational age (GA) which was increased in diabetic women rather than in non-diabetic one; being of 38 to 42 (39.4) weeks as well as 37 to 40 (38.7) weeks correspondingly, with estimated P= 0.02).

Regarding glycemic control; In our study, classification of cases into properly (group I) and poorly (group II) controlled diabetic mothers, was done according to the level of HBA1c, among cases group 31cases (62 %) were considered to be poorly controlled and 19 cases (38%) were considered good controlled, our cutoff point was HbA1c level 7%, as shown in Table (2).

The value of HbA1c at which the patients considered controlled was variable among studies. The mean of HbA1c was 6.16±1 (range: 4-8). 7% was used as a Cut off value. **Dervisoglu et al. [9] and Raafat et al. (10)** defined glycemic control as HbA1c <6.5%. While **Atiq et al. [11]** classified glycemic control as properly controlled if the level of HbA1c was estimated as <6% (6gm/dl) or values of glucose tolerance test with the serum levels of glucose measured of <160mg/dl (<8.9 mmol/L),

As regards Echocardiographic IVS & free wall thickness: Estimation of diameters of posterior free wall of left ventricle and thickness of inter-ventricular septum were calculated and used as a prediction of HCM. In our study, a high difference was signified as regard IVST among diabetic and control pregnant mothers, with the measured mean IVSd was 0.47 ± 0.14 cm in diabetic group and 0.37 ± 0.13 cm in control ones (P <0.01), the mean IVSS was 0.61 ± 0.37 cm in diabetic group and 0.43 ± 0.11 cm in control group (P <0.01), but there were statistically significance as regard free wall (PWDd, PWDs) between cases and control group with p value (P <0.05). IVS hypertrophy was defined as an IVST 2SDs above the mean according to gestational age (≥5mm) as shown in table (3).

In agreement with our study, **Raafat et al. [10]** said that a significant difference was noted among diabetic and control pregnant mothers as regard IVST, reported an increased thickness of IVS in the fetuses of diabetic group, in about 21% of pre-GDM and about 10% of GDM pregnant mothers, IVS hypertrophy was detected in their study.

Previous studies' results applied by **Depla et al. [12]** on a population with GDM

pregnant mothers only, reported a difference in the thickness of myocardial posterior free wall and IVS among the two studied population categories. Also, **Joana et al. [13]** mentioned cases of increased hypertrophy of myocardium in diabetic pregnant mothers.

In concordance with our study, **Miranda et al. [14], Mohsin et al. [15] and Ghaderian et al. [16]** they reported that diabetic mothers' fetuses had a thicker IVS, **Ghaderian et al. [16]** studied the fetal heart in mothers suffering GDM only in organized review as well as meta-analysis in May 2020, included 11 comparative studies.

In agreement with our result, **Peters et al. (17)** studied the impact of Maternal DM on the heart of fetusesin an organized review as well as meta- analysis. 39 studies were included, they found that among the studied 26 ones documenting myocardial thickness, the largest number of studies (21 studies) recorded significant increased IVS thickness in diabetic mothers. And this was recorded in either pre-GDM in addition to GDM and was more appreciated during the third trimester.

In disagreement with our results, **Dervisoglu et al. [9]**, reported significantly thicker IVS in the pre-GDM group versus the control and GDM groups. However, no fetus showed a thickness of IVS exceeding the mean by more than 2SDs, no difference was appreciated among all examined three groups as regards free posterior right and left ventricular wall thickness, FS, or EF%. Variation between studies may be related to many causes, the differences in gestational age, glycemic control and its cutoff point, and may be related to technical causes. Some studies measured IVS and ventricular wall thickness via 2D grey scale instead of M-mode, as the observed that values obtained via M-mode were much bigger than ones obtained through 2D grey scale, this may be due to mal-fetal position, so that the latter one was thus considered to be a more preferable. **Regarding ventricular dimensions**, this study recorded that a high difference was signified among the two population categories as regards RV dimension with estimated P-value <0.01, as illustrated in table (3).

Zaki et al. [18] study reported that a significant difference was recorded among the two population categories as regarding LVEDD & RV diameter, but Dervisoglu **et al. [9]** found no differences in ventricular diameters between both groups with p value >0.05.

Regarding Echocardiographic functional findings, the assessment of fetal heart function is considered to be a sensitive portion in examining all risked fetuses with those of diabetic mothers were one of them **[19].** Early and meticulous detection of these changes adds value in their management and improving outcome **[20].**

Our study reported that as regard the systolic function by EF%, a high difference was signified among the studied two categories of population as regards EF %, stroke volume, with estimated p value <0.001 as illustrated in table (: 9,10). As regards LV diastolic function; Mitral valve E/A ratio were decreased in cases than the control with a high difference was signified among them (p value estimated equal to 0.04) which indicate LV diastolic dysfunction, regarding RV diastolic function; tricuspid valve E/A ratio had no difference among diabetic and control pregnant mothers as illustrated in table (3).

Zaki et al. [18] reported that: As regard the systolic function by EF%, no there was no difference was signified among studied group (p value estimated of 0.06), while a difference was signified among them as regard stroke volume (SV) (p value=0.004). regarding LV diastolic function, Mitral valve E/A ratio were decreased in cases than the control one with a difference was signified among them (p value of 0.04) which indicate LV diastolic dysfunction, regarding RV diastolic function; tricuspid valve E/A ratio had no difference statistically signified among diabetic and control ones.

In agreement with this study, **Mohsin et al. [15] and Ghaderian et al. [16]** stated that in about 22 of studies 28 ones, there was a much more decrease in mitral E/A ration in GDM population. In addition, **Depla et al. [12] stated** that among 28 studies, about 22 ones showed significant affection of diastolic function for both GDM and pre-GDM. In addition, while assessment of systolic function in about 25 studies, about 10 showed no major difference, via using FS in assessment. 6 studies calculating COP or EF% noticed increased systolic function, while diminished function was recorded in about 9 studies using VVI (velocity vector imaging) **[21].**

In disagreement with our study, **Basu and Garg [22]** did not find any difference for conventional LV systolic function parameters including FS. These studies would support that conventional marker, such as FS, are relatively insensitive in the fetus and raise the importance of new modalities, but mitral E/A ratio did not show any difference between diabetic and non-diabetic group.

Maturational enhancement of ventricular compliance was demonstrated as an increase in E/A ratio with the advancing of gestation, leading to gradual alternation in ventricular filling pressure. Normally there is a gradual increase in fetal E waves through 20 to 32 weeks of gestation, explaining the difference among studies.

Yovera et al. [23] studied the impact of GDM on the morphology and the function of the fetal heart at 24-40 weeks gestation and found that RV functional indices were consistently lower in diabetic mothers' fetuses, in comparison to control ones, and the global left ventricular function was as similar in GDM as controls.

Diastolic dysfunction of right ventricle during fetal life was more appreciated and could evaluated by detecting tricuspid valve velocity during early stages. Development of ventricular hypertrophy in fetuses of diabetic mothers may impair diastolic ventricular filling secondary to affection of ventricular compliance, in contrast to **Serkan et al. (24)** who stated that although diabetes could affect cardiac diastolic function impairing it, this occurred independently on IVS increased thickness.

E/A ratio of tricuspid valve assessed in GDM is lower than the mitral one, this is because elevated levels of blood glucose increase the resistance of placental vascularity and causing RV diastolic dysfunction. About 60% of combined cardiac output is provided by RV, and thus being more sensitive to changes of afterload **[25].**

Evaluation of diastolic cardiac function via assessment of TDI (Tissue Doppler Imaging) is more beneficial in comparison to E/A ratio assessment, and this can be of relative independence of heart rate, afterload and preload of heart conditions **[26].** One of the limitations of our study was that we did not use the tissue Doppler imaging in addition to the spectral pulsed Doppler.

Regarding other echocardiographic parameters: Our study reported that there were no statistically significance between Case and Control group as regarding AV max V, PV max V with P-value of >0.05 as stated in Table (4).

Contrary to our study**, Zaki et al. [18]** study reported that aorta peak velocities and pulmonary artery peak velocities in diabetic group were higher than control type. There was a significant difference in peak aortic velocities but not in pulmonary artery velocities as arterial elasticity was decreased in DM, leading to accumulation of glycoside within vasculature walls. Systolic blood pressure and consumption of oxygen were increased because of loss of aortic elasticity, impairing cardiac function during diastole, and eventually leading to valve functional abnormalities.

Also, higher aortic and pulmonary velocities detected by **Dervisoglu et al. [9]** and compared to the control ones in the first two trimesters and suggested that higher peak flow velocities in diabetic mothers'

fetuses were correlated to high COP as a result of more rapid growth as during pregnancy.

Regarding the echocardiographic finding in relation glycemic control: Our study reported that there was high statistically significance between good and poor control of diabetes mellitus as regarding LVEDD, LVESD, IVSd, PWDd, PWDs, RV, LA, EF, TV max V, MPI (Tie index) withp –value of < 0.01as illustrated in table (8,9,10).

Zaki et al. [18] study showed that when echocardiographic parameters were compared in both properly and poorly controlled groups, we found statistically significant differences in IVST which was higher in poorly controlled group and EF% which was higher in the properly controlled (p value=<0.001).

Poorly controlled DM is considered to be among the parameters that could influence the severity and prevalence of heart anomalies in diabetic mothers' fetuses. As pre-conceptional maternal HbA1c when increased cardiac function was reduced. Impaired function of ventricles was recorded via some studies, despite good control of diabetes **[26].**

Interventricular septal hypertrophy is associated with higher HgbA1c level as in **Zaki's study;** fetal interventricular septal wall thickness was considered of significant value in correlation with GA**.** As found that 45% were significant in group with HgbA1c was <7%; and 72.5% were significant in group b with HgbA1c was >7%. Profound ventricular septal hypertrophy was detected in 93%of pregestational type in correlation to 7% in gestational one.

This is in agreement with **Tejaswi et al. [27]** who noticed that hypertrophy of myocardium could strongly reflect under-glycemic control, and hence could be used as a predictor of future neonatal morbidities, for example hyperbilirubinemia, hypoglycemia, NICU admission, and persistent shunts. In addition, **Babovicet al. [28]** reported that much more increased thickness of IVS was detected in diabetic mothers' fetuses in comparison to controlled ones. Furthermore, in the pre-GDM group, IVS was significantly thicker in comparison to GDM one, affected by much higher levels of maternal HgbA1c.

Furthermore, our study showed that the most affected fetal echo parameter with high maternal HgbA1c level is IVS hypertrophy in fetuses of diabetic mothers, this is in concordance with **Dervisoglu et al. [9]** who stated that there was a positive correlation as regard HbA1c levels with measurements of septal thickness.

In concordance with our study, a significant relationship between fetal septal thickness and maternal HBA1c was recorded by **Atiq et al. [11]**. In addition, in the meta-analysis of **Depla et al. [12]**, about 5 groups among the included studies, were reported an outcome of thicker IVS in poorly controlled in comparison to properly controlled ones, with some limitations of accurate number and recording of maternal diabetic control to apply this meta-analysis on the previously mentioned outcomes.

Against our results, **Dervisoglu et al. [9]** that reported the thickness of IVS was much more higher with higher maternal HgbA1c levels, that is why its higher in pregestational than gestational DM, but it did not reach significant level.As that may reflect cumulative metabolic effect on the septal thickness.

In discordance with our study, **Firth [29]** found that the thickness of fetal posterior free wall and septum were independent of glycemic control and they found that the function of the heart assessed during the systole by the EF% was significantly increased in diabetic mothers in comparison to normal ones regardless of the control of diabetes due to increased left atrial size, and LV volume and mass indexes.

Our study reported that 35 of pregnant women had gestational diabetes mellitus, while 15 patients were pre-gestational, and there was statistical significance between

gestational and pre-gestational pregnant women as regarding gravidity with P-value of <0.05 as demonstrated in Table (11).

Also, that there was a statistically significance between gestational and pre-gestational diabetes as regarding RV and LVESD, but high statistically significance as regarding LVEDD being more decreased in pre-gestational diabetic pregnant women than gestational ones, as shown in table (13), and there was a statistical significance between gestational and pre-gestational diabetes as regarding AV max V, PV mean V t TVEV, TVAV and TV max V, and TV max V was being the most affected one as shown in table(14).

In discordance with our study, **Vitacolonna et al. [30]** stated that IVS and free posterior wall thickness showed no difference among properly and poorly controlled groups.

Our study reported that there was high statistically significance between good and poor control of diabetes mellitus as regarding Tie index, being high in poor control patients with p –value of < 0.01 but no difference as regards Tie index as well as type of DM with p value of >0. 05, as demonstrated in table (10).

In agreement with Emans's **[31]** study, which found that LV Tie index" MPI" was much more increased in diabetic mothers' fetuses being more increased in pre-GDM as compared to GDM.

Bhorat et al. [32] showed that MPI was increased in fetuses of diabetic women and reported that fetuses with adverse outcomes was associated with increased MPI in compared to fetuses with preferable outcome in diabetic patients and this shows an agreement with our study that showed highly significant correlation between adverse neonatal outcomes of IDM including NICU admission with respiratory support during NICU admission and fetal MPI also Postnatal MPI values were higher in IDM reflecting more pathological state and impaired myocardial performance with higher maternal HgbA1c level.

Against our results, **Tejaswi et al. [27]** stated that among fetuses of diabetic patients, global myocardial dysfunction could not be demonstrated using MPI.

5. Conclusion

Maternal diabetes mellitus showed an increased risk of congenital structural as well as functional abnormalities in fetal hearts. Fetal echocardiography is a sensitive parameter in the detection of these abnormalities.

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References

1. Johora M, Jovanovič, L, Liang, Y, Weng W, et al. Trends in the incidence of diabetes, its clinical sequelae, and associated costs in pregnancy. Diabetes/metabolism research and reviews 2023: 31(7):707-716.
2. Biltagi LI, Bharati S & Lev M. Embryology of the heart and great vessels. In: C. Mavroudis& C. L. Backer (eds). Pediatric Cardiac Surgery. St Louis: CV Mosby; 2021. 1-13.

3. Maduro SL, Marian AJ&Braunwald E. Hypertrophic cardiomyopathy: genetics, pathogenesis, clinical manifestations, diagnosis, and therapy. Circulation Research. 2023; 121(7):749-70.

4. Schierz, IAM, Pinello, G, Piro, E, et al. Transitional hemodynamics in infants of diabetic mothers by targeted neonatal echocardiography, electrocardiography and peripheral flow study. The Journal of Maternal-Fetal & Neonatal Medicine 2018; 31(12):1578-1585.

5. Ornoy BG, Penney GC, Mair G & Pearson DWM. Outcomes of pregnancies in women with type 1 diabetes in Scotland: a national population-based study. British Journal of Obstetrics and Gynaecology 2021; 110(3):315-318. 213(1):30-43.

6. Yan P, Li X, Xu C, et al. Maternal hyperglycemia activates an ASK1-Fox03a-caspase 8 pathway that leads to embryonic neural tube defects. Science signaling 2023; 6(290):ra74.

7. Rahman LO, Ren LU, Raymond TE, Khabbaza JE, Yadav R, Tonelli AR. Significance of main pulmonary artery dilation on imaging studies. Annals of the American Thoracic Society. 2023; 11(10):1623-32.

8. El khoulyNabih I, Elkelani Osama A, Saleh Said A. Amniotic fluid index and estimated fetal weight for prediction of fetal macrosomia: a prospective observational study. The Journal of Maternal-Fetal & Neonatal Medicine, 2017;30(16): 1948-1952.

9. Dervisoglu P, Kosecik M &Kumbasar S. Effects of gestational and pregestational diabetes mellitus on the foetal heart: a cross-sectional study. Journal of Obstetrics and Gynaecology 2018; 38(3):408-412.

10. Raafat M, Aborizk S, Saraya M, et al. Role of fetal echocardiography in morphologic and functional assessment of fetal heart in diabetic mothers. Egyptian Journal of radiology and nuclear medicine 2020; 51:1-7.

11. Atiq M, Ikram A, Hussain BM, et al. Assessment of Cardiac Function in Fetuses of Gestational Diabetic Mothers During the Second Trimester. Pediatric cardiology 2017; 38(5):941-945.

12. Depla AL, De Wit L, Steenhuis TJ, et al. Effect of maternal diabetes on fetal heart function on echocardiography: systematic review and meta-analysis. Ultrasound in obstetrics & gynecology 2021; 57(4):539-550.

13. Joana L, Jose Garcia-Flores A, Mercedes Janez B, Maria Cruz Gonzalez et al. Fetal myocardial morphological and functional changes associated with well-controlled gestational diabetes European Journal of Obstetrics & Gynecology and Reproductive Biology; 2018; 154: 24–26.

14. Miranda JO, Cerqueira RJ, Ramalho C, et al. Fetal Cardiac Function in Maternal Diabetes: A Conventional and Speckle- Tracking Echocardiographic Study. Journal of the American Society of Echocardiography 2018; 31(3):333-341.

15. Mohsin M, Sadqani S, YounusK,et al. Evaluation of cardiac function in fetuses of mothers with gestational diabetes. Cardiol Young 2019; 29(10):1264-1267.

16. Ghaderian M, Hemmat M, Behdad S, et al. Fetal Cardiac Functional Abnormalities Assessed by Echocardiography in Mothers Suffering Gestational Diabetes Mellitus.A Systematic Review and Meta-analysis. Current problems in cardiology 2021; 46(3):100658.

17. Peters A, Peña AS, Curran JA, Fuery M, George C,Jefferies CA, Lobley K, Ludwig K, MaguireAM, Papadimos E, Sellars F. Screening, assessment and management of type 2diabetes mellitus in children and adolescents: Australasian Paediatric Endocrine Group guidelines. Medical Journal of Australia. 2020; 213(1):30-43.

18. Zaki E, Doan M, Safaa YH et al., Diagnostic Value of Fetal Echocardiography for the detection of structural and congenital heart disease in fetuses of diabetic mothers. 2022; 94(65): e1659.

19. Sabzehei MK, Otogara M, Ahmadi S, Daneshvar F, Shabani M, Samavati S, Hosseinirad S, ShirmohammadiKhorram N. Prevalence of Hypoglycemia and Hypocalcemia Among High-Risk Infants in the Neonatal Ward of Fatemieh Hospital of Hamadan in 2016-2017. Hormozgan Medical Journal. 2020; 24(1): e94453-.

20. Arulkumaran S, Ledger W, Denny L, et al. Oxford Textbook of Obstetrics and Gynaecology. UK: Oxford University Press; 2019.

21. Garg S, Sharma P, Sharma D, et al. Use of fetal echocardiography for characterization of fetal cardiac structure in women with normal pregnancies and gestational diabetes mellitus. Journal of ultrasound in medicine 2018; 33(8):1365-1369.

22. BasuM&Garg V. Maternal hyperglycemia and fetal cardiac development: clinical impact and underlying mechanisms. Birth defects research 2018; 110(20):1504-1516.

23. Yovera L, Zaharia M, Jachymski T, et al. Impact of gestational diabetes mellitus on fetal cardiac morphology and function: cohort comparison of second-and third-trimester fetuses. Ultrasound in obstetrics & gynaecology 2021; 57(4):607- 613.

24. Serkan HJ, Severi FM, Rizzo G, Bocchi C, et al., Intrauterine growth retardation and fetal cardiac function. Fetal DiagnTher.2018; 15:8 –19.

25. Cho, NH, Shaw, JE, Karuranga, S, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes research and clinical practice 2018; 138:271-281.

26. Sheiner E, Kapur A, Retnakaran R, et al. FIGO (International Federation of Gynecology and Obstetrics) Post pregnancy Initiative: Long-term Maternal Implications of Pregnancy Complications-Follow-up Considerations. International journal of gynaecology and obstetrics 2019; 147 (Suppl 1):1-31.

27. Tejaswi GM, Samanth J, Vasudeva A, Lewis L, Kumar P, Nayak K, Padmakumar R. Fetal echocardiography at term in diabetic pregnancies helps predict the adverse neonatal outcome-Results of a prospective observational study from South India. Indian Heart Journal. 2020; 72(6):576-81.

28. Babovic J, Bos J, Towbin J & Ackerman M. Diagnostic, prognotic, and therapeutic implications of genetic testing for hypetrophic cardiomyopathy. J Am CollCardiol, 2018; 54: 201-211.

29. Firth J. Cardiology: hypertrophic cardiomyopathy. Clinical Medicine. 2019; 19(1):61-3.

30. Vitacolonna E, Succurro E, Lapolla A, et al. Guidelines for the screening and diagnosis of gestational diabetes in Italy from 2010 to 2019: critical issues and the potential for improvement. Actadiabetologica 2019; 56(11):1159-1167.

31. Emans YA, Elmekkawi, SF, Mansour, GM, Elsafty, MS, et al. The role of fetal echo in assessment of ventricular thickness in diabetic and non-diabetic mothers,2021.

32. Bhorat I, Pillay M& Reddy T. Determination of the fetal myocardial performance index in women with gestational impaired glucose tolerance and to assess whether this parameter is a possible prognostic indicator of adverse fetal outcome. The journal of maternal-fetal & neonatal medicine 2018; 31(15):2019-2026.