Doppler study of fetal cardiac dysfunction in gestational diabetes and its effect on perinatal outcome

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SUMMARY

AUTHORS' CONTRIBUTION: **(A)** Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

Background: Diabetes in pregnancy is unique because of the diversity of problems that can affect fetus beginning with conception. Babies born to diabetes mothers commonly have heart damage. Whether this is caused by inadequate glucose regulation is still up for debate.

Objective: To correlate Doppler study of fetal ductus venosus, IVC and interventricular septum thickness with fetal cardiac dysfunction in controlled and uncontrolled diabetic pregnancy.

Methods: This study included 200 women from diabetes (N=140) and non-diabetes (N=60). Both groups are with singleton pregnancies without major malformations. They classified into: group I (N=60 women with normal pregnancies), group II (N=60 women with controlled diabetes) and group III (N=80 women with uncontrolled diabetes). Diagnostic criteria of maternal diabetes mellitus followed American College of Obstetricians and Gynecologists Guidelines. For all women, the following was done: Routine history taking, general, obstetric examination, routine investigations, ultrasound scanning of fetal viability, and measurement of cardiac interventricular septum thickness (the 4-chamber view), Doppler velocimetry (P/I) for of ductus venosus and APGAR score.

Results: The following were statistically significant difference. in group III, The femur length, the head circumference, the abdominal circumference, and AFI was significantly greater than that in groups I and II. Group III had a statistically significant mitral E wave peak flow than groups I and II. Group III had a statistically significant tricuspid E wave peak flow than groups I and II.

Conclusion: Fetuses of mothers with uncontrolled diabetes have impaired in ductus venosus flow with an increase in the pulsatility index of that flow as compared with fetuses of mothers with controlled diabetes and normal fetuses of non-diabetic mothers. It can be used for assessment of diastolic dysfunction in fetuses of diabetic mothers.

Keywords: Doppler; Cardiac dysfunction; Gestational diabetes

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INTRODUCTION

Pregnancy-related diabetes carries dangers for both the mother and the growing foetus. An increased risk of negative pregnancy outcomes, such as miscarriage, foetal congenital abnormality, and neonatal death, exists in women with type 1 and type 2 diabetes [1].

Congenital malformation rates in diabetic mothers treble or triple compared to rates in the general population, and they are inversely related to first-trimester glucose control, according to level I evidence [2].

Due to foetal hyperinsulinemia and an increase in the number of insulin receptors in the heart, which results in an increase in protein and fat synthesis and causes myocardial cells to hyperplasia and hypertrophy, maternal diabetes causes changes in the body [3].

Foetal myocardiac hypertrophy is the most common anomaly in newborns of mothers with diabetes is, which can be seen in up to 35% of such children. The ventricular septum appears to have a very high concentration of insulin receptors, which may account for the more pronounced hypertrophy of that structure. The left ventricular filling changes between the 20th and 36th trimester weeks in diabetic foetuses in addition to myocardial hypertrophy [4].

Doppler echocardiography, which uses curves that link the timing and speed of ventricular filling, is a suitable noninvasive technique for assessing diastolic function. Reduced ventricular compliance in foetuses of diabetes mothers may result from thickening of the ventricular wall or from other causes, such as metabolic changes in the uterine environment linked to qualitative changes in collagen (an increase in the fluorescent collagen in the myocardium) [5].

Ultrasound is the preferred imaging method. It is easily accessible, largely regarded as a "familiar test" by patients, and is reasonably priced. The test performed to identify heart problems in foetuses is called foetal echocardiography. Echocardiography plays a crucial role in prenatal diagnosis, and its reliability and safety have both been thoroughly proven. The inspection is difficult and time-consuming due to the small features in these images and the fetus's erratic movements. Despite these obstacles, foetal echocardiography has given clinicians a better understanding of foetal hemodynamics and an earlier diagnosis of cardiac disease [6].

AIM OF THE WORK

The aim of this work is to study Doppler of fetal cardiac dysfunction in gestational diabetes and its effect on perinatal outcome.

PATIENTS AND METHODS

This cross-sectional observational study was conducted during the period from April 2020 to March 2022. Two hundred women (140 diabetics and 60 with normal pregnancy) were included in the study.

Patients:

The included patients were classified into:

Group I: 60 women with normal pregnancies

Group II: 60 women with controlled diabetes.

Group III: 80 women with uncontrolled diabetes.

Inclusion criteria:

1. Singleton pregnancies.
2. No major malformations.
3. Gestational age ranging between 32 to 40 weeks.
4. Criteria of controlled diabetics:
a. Preprandial blood sugar level is 70-100 mg/dl.
b. Postprandial blood sugar level is 126-140 mg/dl.
c. Glycosylated hemoglobin (HbA1c) is < 7.
5. Patient agreement and informed written consent for participation in the study.

Methods:

For all women, all women were subjected to Routine history taking, general, obstetric examination, and routine investigations.

Routine ultrasound examination and Doppler study of the fetoplacental circulation:

- Ultrasound scanning of fetal viability, biometry maturity, placental site and fetal biophysical profile, exclusion of major congenital anomalies and measurement of cardiac interventricular septum thickness and right ventricular and left ventricular wall thickness in the 4-chamber view.
- The septum is considered hypertrophied if its measurement exceeds 6 mm and the ventricular wall is considered hypertrophied if its measurement exceeds 5 mm.
- Doppler velocimetry (P/I) was done for ductus venosus.
- Ultrasonographic examinations and Doppler blood

flow study were performed using Voluson730 Pro V unit (GE healthcare, Zipf, Austria) equipped with a broad band multifrequency convex probe 3.5/7MHz.

- Abnormal venous Doppler flow was defined as Ductus venosus PIV above the 95th percentile.
- Patients were subjected to periodic ultrasound and Doppler examinations according to the standard protocol. The interval between exams was primarily determined by the maternal condition and the result of the last Doppler exam.
- In all patients, the last Doppler ultrasound exams were performed within 24 hours before delivery. Only the last measurement before delivery was included in the statistical analysis.

Outcomes

Pregnancy outcomes:

Immediate pregnancy outcomes obtained were:

a. Gestational age at delivery
b. Onset of labor: spontaneous or induced
c. Mode of delivery.

Neonatal outcomes:

a. Apgar score at 1 and 5 minutes
b. Birth weight
c. Admission to neonatal intensive care unit (NICU)

Statistical analysis: Epi-Info version 6 and SPP for Windows version 8 were used to enter, verify, and analyse data.

RESULTS

During the study period (April 2020 – March 2022), 200 women were eligible for inclusion in the study and available for statistical analysis. Of these, 140 were diabetics and 60 were with normal pregnancy. Patients were grouped as follows:

- Group I: It included 60 women with normal pregnancies.
- Group II: It included 60 women with controlled diabetes.
- Group III: It included 80 women with uncontrolled diabetes.

Our results showed that:

Comparing the clinical characteristics between the three groups, no significant differences were found regarding age and parity. Patients with diabetes (groups II and III) had significantly higher blood sugar level than those with normal pregnancies (group I). Gravidity, number of previous abortions and gestational age showed

no significant differences between the three groups as shown in **Tab. 1**.

Non-significant differences were found between the three groups regarding the mode of delivery and indications of cesarean section although group I showed slight increase in the rate of cesarean section (**Tab. 2.**) the frequency of admission to the NICU were highly significant between the three groups. In group III, and admission to the NICU was significantly higher than groups I and II. In addition, group II showed significant differences regarding the same variables in comparison to group I (**Tab. 3.**). Femur length in group III was significantly higher than groups I and II (p < 0.001), no difference in biparietal diameter was found between the three groups (p < 0.001), head circumference was significantly higher in group III than groups I and II (p < 0.001), abdominal circumference was significantly higher in group III than groups I and II (p < 0.001), AFI was significantly higher in group III than groups I and II (p < 0.001) as shown in **Tab. 4.**

The mean pulsatility index was significantly higher in group III than in groups I and II (p < 0.001). Comparing the pulsatility index of ductus venosus in group I with

that in group II, a statistically significant difference (p = 0.02) was observed as shown in **Tab. 5**. The means of the septal thicknesses and the right and left ventricular walls are shown in **Tab. 6**. There were highly significant increase in septal thickness, right ventricular wall and left ventricular wall thickness in group III compared with the other two groups (this presents cardiac dysfunction and cardiomyopathy) (**Tab. 6.**).

There were statistically high significant differences among the studied groups regarding Apgar score (p < 0.001) and admission to NICU (**Tab. 7.**). There were statistically high significant differences among the studied groups regarding cardiomyopathy (p < 0.001) except for RV which exhibited a significant difference (**Tab. 8.**). There were statistically high significant relations between cardiomyopathy and neonatal outcome (**Tab. 9.**).

DISCUSSION

According to some research, sonographic evidence of abnormal heart function is visible before ultrasounds show evidence of cardiac structural abnormalities [7].

Preload and afterload can both impact the parameters of

Tab. 1. Comparison of the 3 groups with relevant data.

Variables	Group I (n = 60)		Group II (n = 60)		Group III (n = 80)		X²	P
	No	%	No	%	No	%		
Age (years)	24.7 ± 5.6		25.3 ± 5		26.2 ± 5.4		0.69	0.49 (NS)
Parity	2 ± 1.3		2.3 ± 1.4		1.9 ± 1.2		0.42	0.85 (NS)
Blood sugar level	90 ± 6.5		160 ± 10.6		190 ± 10.8		939	< 0.001 (HS)
Gravidity								
≤ 2	40	66.7	42	70	40	50	3.46	0.17 (NS)
> 2	20	33.3	18	30	40	50		
Number of previous abortions								
No	46	76.7	52	86.7	52	65	4.36	0.11 (NS)
Yes (1-3)	14	23.3	8	13.3	28	35		
Gestational age (weeks)								
Mean ± SD	38.8 ± 1.3		38 ± 1		35.9 ± 1.4		F = 50.1	< 0.001 (HS)
Range	20-34		20-34		28-34			

Tab. 2. Mode of delivery and indications of cesarean section.

Variables	Group I (n = 60)		Group II (n = 60)		Group III (n = 80)		P
	No	%	No	%	No	%	
Vaginal delivery	44	73.3	36	60	40	50	0.14 NS)
Cesarean section	16	26.7	24	40	40	50	
Fetal distress	6	37.5	8	33.3	8	20	0.78 NS)
Failed progress	2	12.5	6	25	8	20	
Previous CS	8	50	8	33.3	18	45	
Oversized baby	0	0	2	8.3	6	15	

Tab. 3. Comparison of perinatal outcome among diabetic women.

Variables	Group I (n = 60)		Group II (n = 60)		Group III (n = 80)		P value
	No	%	No	%	No	%	
Polyhydramnios	4	6.7	24	40	48*	60	< 0.001 (HS)
Gestational age at delivery (weeks)	39 ± 1.3		38 ± 1		36* ± 1.4		< 0.001 (HS)
Birth weight (gm)	3 ± 0.62		3.5 ± 0.63		4.3 ± 0.4		< 0.001 (HS)
Admission to NICU	4	6.7	8	13.3	28*	40	< 0.001 (HS)

+p < 0.001 comparing groups I and II; *p < 0.001 comparing groups I and III; *++p < 0.001 comparing groups II and III; p value is determined by Chi square except birth weight determined by analysis of variance.

Tab. 4. Fetal biometry and amniotic fluid index among the 3 groups.

Variables	Group I (n = 60)	Group II (n = 60)	Group III (n = 80)	F	p
Femur length (mm)					
Mean ± SD	75 ± 1	74 ± 0.5	77 ± 1	106.3	< 0.001 (HS)
Biparietal diameter (mm)					
Mean ± SD	93 ±1	91 ± 0.7	94 ± 0.3	132	< 0.001 (HS)
Head circumference (mm)					
Mean ± SD	345 ± 3	343 ± 3	347 ± 5	8.37	< 0.001 (HS)
Abdominal circumference (mm)					
Mean ± SD	335 ± 53	343 ± 2	349 ± 2	96.7	< 0.001 (HS)
AFI (cm)					
Mean ± SD	13.9 ± 2	17 ± 3	22 ± 3	78.2	< 0.001 (HS)

Tab. 5. Ductus venosus PI.

Variables	Group I (n = 60)	Group II (n = 60)	Group III (n = 80)	F	P
DV PI					
Mean ± SD	0.6 ± 0.1	0.8 ± 0.2*	1.3 ± 1*	12.7	< 0.001 (HS)
Range	0.5-0.9	0.6-1.1	0.9-2.6		

Tab. 6. Cardiac biometry.

Variables	Group I (n = 60)	Group II (n = 60)	Group III (n = 80)	F	p
Ventricular septum (mm)					
Mean ± SD	2.6 ± 0.7	3 ± 0.6	6.4 ± 2*	84.1	< 0.001 (HS)
Range	1.3-3.5	1.5-3	04-13		
RT ventricular wall (mm)					
Mean ± SD	3 ±1	4 ± 1	5.5 ± 1*	55.5	< 0.001 (HS)
Range	02-05	02-04	4.5-6.5		
LT ventricular wall (mm)					
Mean ± SD	3 ± 1	3 ± 1	5 ± 1*	48	< 0.001 (NS)
Range	1.5-5	02-04	4.5-8		

Tab. 7. Neonatal outcome among the studied groups.

Variables	Group I (n = 60)		Group II (n = 60)		Group III (n = 80)		X²	P
	No	%	No	%	No	%		
Admission to NICU	0*	0	20	33.3	28	35	13.56	0.0011* (S)
Apgar score(at one min)								
Mean ± SD	8* ± 0.7		5.4 ± 0.9		5.1 ± 1.2		F = 83.9	< 0.001 (HS)
Range	06-09		04-07		03-07			
Apgar score(at five min)								
Mean ± SD	9* ± 0.7		8.4 ± 0.9		7.1 ± 1.2		F = 83.9	< 0.001 (HS)
Range	07-09		04-07		03-07			

Tab. 8. Distribution of cardio-myopathy among the studied groups.

Variables	Group I (n = 60)		Group II (n = 60)		Group III (n = 80)		X²	P
	No	%	No	%	No	%		
Septal thickness	0	0	0	0	18	22.5	14.84	< 0.001 (HS)
RV	0	0	0	0	16	20	13.04	0.0014 (S)
LV	0	0	0	0	16	20	13.04	0.001 (HS)
Both RV and LV	0	0	0	0	22	27.5	18.54	< 0.001 (HS)
Total (septal + LV + RV) (cardiomyopathy)	0	0	0	0	36	45	32.93	< 0.001 (HS)

cardiac performance, making the research of foetal cardiac function complicated. Despite the fact that Baschat et al., looked only at cardiac performance metrics without taking afterload and preload into account, Doppler approaches for assessing first-trimester heart function have previously been reported [8].

Compared to foetuses of mothers with normal pregnancies (group I) and foetuses of mothers with controlled diabetes (group II), foetuses of mothers with uncontrolled diabetes (group III) had a significantly higher ductus venosus pulsatility index (DVPI) (group II).

Similar findings were made by Zielinsky et al., who discovered that PIDV is considerably higher in foetuses of diabetic mothers (FDMs) with maternal hyperglycemia

Tab. 9. Relation between cardiomyopathy and neonatal outcome.

Variables	Thickness				X^2	P
	-ve		+ve			
	No	%	No	%		
Admission to NICU	10	12.2	14	77.8	31.3	< 0.001 (HS)
Apgar < 5	25	30.5	16	88.9	20.81	< 0.001 (HS)
Ductus PI	8	9.75	14	77.8	35.93	< 0.001 (HS)

(MH) compared to FDMs without MH and foetuses of non-diabetic mothers (FNDM). The Ductus Venosus Peak Velocity Index for Veins (DV-PVIV) was found to have 53.3% sensitivity, 74.6% specificity, 32% positive predictive value, and an 87.7% negative predictive value for predicting adverse perinatal outcomes in pregestational diabetic pregnancies, according to Wong et al. (2019) who also showed similar results but with a different index [9-11].

In foetuses of pregestational diabetes women with normal cardiac morphology, Turn et al., examined first trimester foetal cardiac performance. They had the express goal of assessing the correlation between cardiac performance metrics and the degree of hyperglycemia while taking into consideration potential additive effects of preload and afterload. They came to the conclusion that compared to non-diabetic controls, foetuses of poorly controlled diabetic moms have substantial abnormalities in first trimester diastolic cardiac function. With rising HbA1c, the decline in myocardial function becomes more pronounced and doesn't seem to be affected by preload or afterload [12].

In order to characterise the foetal cardiac anatomy and function in both healthy pregnancies and pregnancies complicated by GDM, Ren et al., used two-dimensional US, pulsed wave Doppler, and they assessed the impact of glycemic control on the results. They came to the conclusion that diastolic function was compromised and foetal heart wall thickness was increased in women with controlled or uncontrolled GDM [13].

According to Pietryga et al., aberrant placentation can cause chronic intrauterine hypoxia, which can impair foetal cardiac function and make diabetic foetuses more vulnerable to an acute hypoxic insult [14,15].

According to the results of another study, foetal cardiovascular development is crucial for a healthy pregnancy and has an impact on adults as well. Maternal hyperglycemia can have a number of significant effects on the foetal cardiovascular development, making it difficult for women to maintain healthy blood sugar levels during normal pregnancy. One important aspect that affects these consequences is the timing and intensity of hyperglycemia relative to gestational age. First trimester hyperglycemia in pre-gestational diabetes affects organogenesis and can cause the normal congenital heart problems [16].

According to another study, the foetus is at risk for cardiac hypertrophy and subsequent myocardial dysfunction starting in the second trimester. These foetuses have a five times higher chance of stillbirth than the general population [17,18].

CONCLUSION

In the present study, we concentrated on the late gestations because they may have significant clinical relevance in the prenatal detection of septal hypertrophy among the foetuses of diabetic mothers.

In conclusion, mothers with uncontrolled diabetes show poorer ductus venosus flow and an increase in the pulsatility index of that flow. It can be used to evaluate the diastolic dysfunction in those foetuses.

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