

Original Article

A Cross Sectional Study of Fetal Heart Parameters in Gestational Diabetes Mellitus

Charishma Halemani¹, Santosh S Basarakod², Suvarna Guled³, Chaitra N⁴

Abstract

Background : GDM is associated with increased fetomaternal morbidity and mortality. It is estimated that 1 in 4 births are affected by GDM. Constant exposure to high levels of maternal glucose in the intrauterine period, leads to hyperglycemia and hyperinsulinemia in the fetus, resulting in altered organogenesis and growth. A condition known as fetal hypertrophic cardiomyopathy, is common in these fetuses and is characterized by asymmetric myocardial hypertrophy affecting the interventricular septum. This change does not pose a risk to the fetus unless associated with functional impairment. Thus, it is important to monitor pregnant diabetic women for fetal cardiac dysfunction. Echocardiography is a non-invasive, widely available, accurate screening tool for evaluation of fetal cardiac structure and function. Hence, this study was undertaken to contribute to recognizing the importance of fetal heart surveillance parameters in GDM.

Materials and Methods : This is a prospective observational study conducted on 150 pregnant women at a tertiary centre in Western Maharashtra from January, 2019 to December, 2021. Women with singleton, uncomplicated pregnancy with Gestational Diabetes Mellitus were included. Fetal echocardiography was done between 24-28 weeks of gestation and ventricular wall thickness, interventricular septum thickness, ejection fraction, E/A ratio, systolic and diastolic functions were assessed and analyzed.

Results : The Mean age of the women with GDM was 27.63 years and mean period of gestation was 25.57 weeks. The mean RV wall thickness, LV wall thickness and IVS thickness was 3.2 mm, 3.5 mm and 3.7 mm respectively. Mean LVEF% was 69.08%, TV E/A ratio 0.7 and MV E/A ratio was 0.8. Normal LV diastolic function was seen in 14.6% cases, while mild, moderate and severe LV diastolic dysfunction was seen in 52.6%, 32% and 0.8% cases respectively. Normal RV diastolic function was seen in 26.6% cases, while mild, moderate and severe RV diastolic dysfunction was seen in 34.6%, 38% and 0.8% cases respectively. Neonatal echo was indicated in 49.3% cases while congenital anomalies were present in 9.3% cases.

Conclusion : The present study found an increased interventricular septum among the fetus of mothers with gestational diabetes with no significant cardiac dysfunction.

Key words : Gestational Diabetes Mellitus, Fetal Echocardiography, Cardiac Dysfunction.

Globally, the prevalence of diabetes is increasing at an alarming rate. The number is expected to rise from 536.6 million to 783.2 million by 2045¹. The shift in the work – life balance, sedentary lifestyle, food habits and reduced physical activity has increased the burden of obesity and diabetes in

Editor's Comment :

- Fetal hypertrophic cardiomyopathy is common in pregnancy with gestational diabetes. Though the condition is asymptomatic with no significant cardiac dysfunction, it is important to monitor the fetus in gestational diabetes mellitus. Echocardiography is a reliable, safe, non-invasive method for the monitoring of the fetus.

¹MBBS, MS, CMO, Imphal, Department of Obstetrics and Gynecology, Assam Rifles, Imphal, Manipur

²MBBS, MS, Senior Resident, Department of Obstetrics and Gynecology, Bharat Ratna Dr B R Ambedkar Medical College, Bangalore, Karnataka 560045

³MBBS, MS, Assistant Professor, Department of Obstetrics and Gynecology, Sri Siddhartha Medical College, Tumakuru, Karnataka 572107

⁴MBBS, MS, Assistant Professor, Department of Obstetrics and Gynecology, Bharat Ratna Dr B R Ambedkar Medical College, Bangalore, Karnataka 560045 and Corresponding Author

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reproductive age group, thus increasing the occurrence of hyperglycemia in pregnancy. The overall prevalence of GDM is between 4-16.5% worldwide².

Gestational Diabetes Mellitus (GDM) is any degree of glucose intolerance during the pregnancy and is characterized by onset or first detection in the present pregnancy³. Thus, new onset diabetes in pregnancy

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as well as unrecognized pre-gestational diabetes are included in the definition. Women with GDM develop short term pregnancy complications like pre-eclampsia, cesarean delivery, macrosomia, still birth, shoulder dystocia. In future, there is increased risk of developing type 2 diabetes, cardiovascular problems. About half of the women with history of GDM develop type 2 diabetes in 10 to 20 years after delivery⁴. GDM also has genetic implications, meaning that offspring are at higher risk of obesity, diabetes, hypertension and metabolic syndrome. It is estimated that one in four births are affected by gestational diabetes⁵.

In India, the prevalence of GDM varies from region to region, mainly attributed to cultural difference, food habits, socio-economic status and demographic factors. The prevalence in rural areas of central⁶ and western⁷ India is 1.9% and 12.7% respectively, which is much higher in urban areas, higher socioeconomic status and older age groups⁸. There is also variation in the incidence of GDM, depending on the criteria used for the diagnosis, accordingly it is 22.64% with IADPSG criteria, 17.61% with modified Carpenter and Coustan and 13.21% with DIPSI⁹.

Constant exposure to high levels of maternal glucose in the intrauterine period, leads to hyperglycemia and hyperinsulinemia in the fetus. As the intrauterine growth of fetus is dependent on insulin-like growth factors (IGF-1), increased insulin and endogenous catecholamines levels exert an anabolic effect, resulting in altered organogenesis and growth¹⁰. Hyperglycemia has a teratogenic effect on heart and leads to myocardial remodeling which may manifest as cardiomyopathy, microvascular protrusions and subcellular issues¹¹. A condition known as fetal hypertrophic cardiomyopathy, is common in these fetuses and is characterized by asymmetric myocardial hypertrophy affecting the interventricular septum. It is believed to be the result of fetal hyperinsulinemia and increased insulin receptors expression and affinity which leads to the proliferation and hypertrophy of cardiac myocytes¹². These changes do not pose a risk to the fetus unless they are related to functional impairment. Therefore, it is important to monitor pregnant diabetic women for fetal cardiac dysfunction¹³.

In recent years, fetal echocardiography has gained popularity and is widely used to evaluate fetal cardiac anomalies¹⁴. It is a simple, effective and non-invasive technique. Addition of doppler studies, has given an

insight into the better understanding of the fetal cardiac function. Diastolic dysfunction is the earliest change of fetal hypertrophic cardiomyopathy with GDM, which can be detected by the fetal echocardiography¹⁵. The non-invasive nature and wide availability of fetal echocardiography makes it a good screening tool in the low resource country for the evaluation of cardiac function and detection of structural congenital cardiac defects. Hence, the study was undertaken at our tertiary care centre to contribute in recognizing the importance of fetal heart surveillance parameters in gestational diabetes mellitus.

MATERIALS AND METHODS

This prospective observational study included 150 pregnant women in a Tertiary Care Centre in Western Maharashtra from January, 2019 to December, 2021. Pregnant women with singleton, uncomplicated pregnancy with gestational diabetes mellitus were included in the study. Pregnant women with pre-gestational diabetes, multiple pregnancy, fetal structural or chromosomal abnormalities and those with medical and obstetric co-morbidities were excluded from the study.

After obtaining an informed consent, medical history and physical examination was done as per a piloted proforma. Maternal information such as age, height, weight, body mass index, gravidity, parity, gestational age and diabetes treatment were noted. The fetal echocardiography was performed by experienced personnel according to American Society of Echocardiography guidelines between 24 to 28 weeks of gestation. Using the Epiq 7 Bothell Ultrasound system for the fetal echo-cardiography, the thickness of the fetal ventricular walls and interventricular septum was measured. Repeat scan after 4 weeks was performed in cases with a suboptimal echocardiographic window or a suspicion of a lesion. Ventricular wall thickness, interventricular septum thickness, ejection fraction, E/A ratio were noted. Both the systolic and diastolic functions were assessed and the parameters were noted. All the neonates with a suspicion or abnormal echocardiographic features were subjected to echo-cardiography at birth.

The sample size was calculated taking into consideration various fetal echocardiographic characteristics with α error of 5%-10% and confidence interval of 95%, the required sample size is shown in

Table 1 — Sample size estimation

Fetal echocardiography characteristics	Mean	SD	α error	Required sample size
IVS thickness (mm)	3.2	0.1	5%	15
RV wall thickness (mm)	3.29	0.59	10%	134
LV wall thickness (mm)	3.41	0.57	10%	125
RV EF (%)	0.26	0.16	5%	39
LV EF (%)	0.25	0.12	5%	22
Tricuspid E/A	0.66	0.18	5%	50
Mitral E/A	0.72	0.12	5%	22

Table 1. Thus, 150 subjects were included in the present study.

The quantitative data is presented as mean and Standard Deviation and the qualitative data is presented as frequency and percentage. Appropriate statistical software, including but not restricted to MS Excel, SPSS version 20 were used for statistical analysis.

RESULTS

The mean age of the women in the present study was 27.63 years and the mean period of gestation at the time of foetal echocardiography was 25.57 weeks. Majority were primigravida (44.7%), followed by G2 (34.7%) and G3 (12.7%). 50% (75) of the women were graduate. Among the mothers, there were 11(7.3%) who had past history of gestational diabetes and 32(21.3%) had family history of diabetes.

As shown in Table 2, the mean FBS was 100.59±17.549. The majority of the mothers had HbA1c within 6.5 and there were 7(4.6%) who had HbA1c more than 6.5. The oral glucose tolerance test showed 18(12%) levels less than 92mg/dl at 1 hour and 126 (84%) had ≤180mg/dl at 2 hours and 127(84.7%) had ≤153mg/dl levels at 3 hours. 22.7% (34) women were managed on MNT, while 44.4%(65) were on MNT + OHAs. 10%(15) women required insulin and 16%(24) required both OHAs and insulin.

Table 2 — Baseline maternal characteristics

Parameters (n=150)	Minimum	Maximum	Mean	SD
Age (in years)	19	38	27.63	4.107
Period of gestation (in weeks)	23	35	25.57	1.891
Weight (in kg)	41	95	66.03	10231
Height (in cm)	127	165	155.8	4.421
BMI	17	43.47	27.23	4.28
Blood glucose values :				
Fasting (mg/dl)	72	202	100.59	17.549
Post prandial (mg/dl)	88	202	132.19	21.613
HbA1C (%)	4	7.9	5.592484	0.645795

In our study, the mean Right Ventricular wall thickness was 3.2 mm, mean Left Ventricular wall thickness was 3.5 mm and the mean Inter Ventricular Septal thickness was 3.7 mm. The detailed structural parameters are shown in Table 3.

The normal blood flow into the ventricles consists of a biphasic waveform in which the initial flow coincides with the E- wave which is the passive filling period of the ventricle and the late flow coincides with the A-wave. The functional parameters of our study are shown below (Table 4).

Congenital anomalies were present in 9.3% (14) cases. The commonest anomalies seen were the renal anomalies like dilated renal pelvis, pyelectasis

Table 3 — Structural parameters of fetal echocardiography

Parameters (in mm)	Number	Percentage
Right ventricular wall :		
2.5 to 3	34	22.7
3.1 to 3.5	92	61.3
3.6 to 4	22	14.7
>4	2	1.3
Left ventricular wall :		
2.5 to 3	3	2
3.1 to 3.5	85	56.7
3.6 to 4	50	33.3
>4	12	8
Inter ventricular thickness :		
2.5 to 3	3	2
3.1 to 3.5	41	27.3
3.6 to 4	75	50
>4	31	20.7

Table 4 — Functional parameters of fetal echocardiography

Parameters (n=150)	Mean	SD
LV EF %	69.08	2.606
TV – E (m/s)	36.48	6.347
TV – A (m/s)	47.10	7.727
TV – E/A ratio	0.774	0.421
MV – E (m/s)	39.35	6.946
MV – A (m/s)	48.33	7.881
MV – E/A ratio	0.814	0.481
Parameters	Number	Percentage
LV diastolic dysfunction :		
Normal	22	14.6
Mild	79	52.6
Moderate	48	32
Severe	1	0.8
RV diastolic dysfunction :		
Normal	40	26.6
Mild	52	34.6
Moderate	57	38
Severe	1	0.8

(LV- Left Ventricle, RV- Right Ventricle, TV- Tricuspid Valve, MV – Mitral Valve, EF – Ejection Fraction, E – E Wave, A – A Wave, SD – Standard Deviation)

of kidneys. Echogenic focus in the LV were the commonest cardiac defects. Two babies also had small mid muscular VSD detected on fetal 2D echocardiography. Choroid plexus cyst was the nervous system anomaly commonly encountered. Neonatal echocardiography at birth was indicated in 49.3% (74) cases due to either suboptimal echocardiographic window or a suspicion of a lesion during fetal echo.

DISCUSSION

In our study, the mean age of the women was 27.63 years and BMI was 27.23 kg/m². The mean period of gestation at the time of ultrasonography was 25.57 weeks. In Pooransari P, *et al*¹⁶ study, the mean age was 29.59 ± 5.52 years, mean BMI of 26.36 ± 0.41 kg/m² and mean gestational age was 23 ± 3.4 weeks (median: 22 weeks). In our study, mean FBS was 100.59 while mean postprandial blood sugar was 132.19, mean HbA1c was 5.59%. The majority of the mothers with GDM was well controlled while 4.6% had poorly controlled GDM.

The effect of maternal hyperglycaemia on the developing fetal heart is complex and multifactorial. During the period of organogenesis, persistent hyperglycaemia leads to increased apoptosis, cell homeostasis, proliferation and migration of neural crest cells, thus affecting the heart and neural tube development¹⁷. In later gestation, hyperglycaemia attenuates the angiogenic capability of surviving endothelial cells, thus modifying the cardiac function and morphology by controlling total cardiomyocyte number¹⁸. Hypertrophic cardiomyopathy is a common structural abnormality seen in diabetic mothers, accounting upto 40% of cases¹⁹. It is characterised by thickening of interventricular septum and free ventricular wall. In our study, according to structural parameters mean RV wall thickness was 3.2 mm, mean LV wall thickness was 3.5 mm while mean IVS thickness was 3.7 mm. In Peng Y-Q, *et al*²⁰ study, the interventricular septum thickness was 2.76 ± 0.55mm which was significantly thicker in GDM group than the control group. Dervisoglu P, *et al*¹³ study also observed that in diabetic group, the fetal Interventricular Septum (IVS) thickness was significantly greater than in non-diabetics ($p < 0.05$) but none had an IVS >2 SD from normal. Ghandi Y, *et al*²¹ study found using M-mode echocardiography, Interventricular Septum Thickness (IVS) and LV mass

were significantly higher in GDM than control group.

A conventional echocardiographic method to measure the diastolic function is to analyse the flow velocities across the Atrioventricular Valve (AV) using pulsed wave doppler which is expressed as E/A ratio. E wave represents the early passive filling velocity caused by ventricular relaxation, while A wave represents the active filling velocity caused by atrial contraction in late diastole²². Mitral and tricuspid valve E/A ratio helps to assess the cardiac compliance and preload conditions. It was observed in our study that mean LVEF was 69.08%, mean TV E/A ratio was 0.774 ± 0.421 and mean MV E/A ratio was 0.814 ± 0.481. These findings were comparable to Karaca Kurtulmus S *et al* study²³ where the TV E/A ratio was 0.7576 ± 0.1282 and MV E/A ratio was 0.7982 ± 0.1140 in GDM group. Similarly, Hou, *et al*²⁴ study found that mitral valve E/A ratio was 0.637 ± 0.045 and tricuspid valve E/A ratio was 0.702 ± 0.067 in GDM fetus and there was no significant difference seen in mitral or tricuspid valve E/A ratio between the GDM and control groups. Mohsin M, *et al*²⁵ study observed mitral E/A ratio was lower in gestational diabetes group as compared to the control ($p < 0.001$).

In the present study, normal LV diastolic function was seen in 14.6% cases, while mild, moderate and severe LV diastolic dysfunction was seen in 52.6%, 32% and 0.8% cases respectively. Also, normal RV diastolic function was seen in 26.6% cases, while mild, moderate and severe RV diastolic dysfunction was seen in 34.6%, 38% and 0.8% cases respectively. Miranda JO, *et al*¹⁵ showed that diastolic function seemed to be impaired in the right ventricle, with the diabetic group presenting more negative longitudinal early and late diastolic strain rates. Depla AL, *et al*²⁶ study found a strong association between maternal diabetes and impaired fetal cardiac function in diabetic mothers and concluded that functional changes can occur in the absence of cardiac hypertrophy and also in pregnancies with good glycemic control.

CONCLUSION

The present study found an increased interventricular septum among the foetus of mothers with gestational diabetes. The existing nomograms of the fetal cardiac dimensions in the literature are based on the western population. The Indian population do not have the appropriate nomograms. This study will add to the database and may contribute to the research in future

and also aid in preparation of a similar nomogram for the South East Asian population in the upcoming years.

Ethical Clearance : The study was approved by the Institutional Ethical Clearance Committee.

Conflict of Interest : None declared

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