M Mode Assessment of Fetal Interventricular Septal Thickness in Third Trimester with Comparison Between Diabetic and Non-Diabetic Mothers

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KEYWORDS
Interventricular septal thickness, gestational diabetes, congenital heart abnormality, fetus.

ABSTRACT
Background: Babies born to diabetic mothers face increased risks of illness and death despite advances in prenatal care. One common heart defect in these babies is interventricular septal hypertrophy.
Objective: This study examines how gestational diabetes affects fetal interventricular septal thickness (IVST).
Material & Methods: The study took place at Sharda Hospital's Radiology Department over two months. Ninety pregnant women between 28 and 35 weeks of gestation were selected. The women were grouped based on oral glucose tolerance test (OGTT) results into non-diabetic (Subgroup A), controlled diabetic (Subgroup B), and uncontrolled diabetic (Subgroup C). IVST measurements were taken using M-mode during diastole.
Results: The average age of participants was 26.41±3.18 years. In the 28-32 week group, the mean IVST was 3.76±0.23mm for non-diabetic women, 4.00±0.28mm for controlled diabetics, and 5.83±0.64mm for uncontrolled diabetics. In the 32-35 week group, the mean IVST was 4.25±0.29mm for non-diabetics, 4.75±0.43mm for controlled diabetics, and 6.84±0.34mm for uncontrolled diabetics. IVST was significantly higher in uncontrolled diabetics ($p<0.05$), while non-diabetic and controlled diabetic groups had similar thicknesses. There was a significant positive correlation between OGTT levels and IVST ($p<0.05$).
Conclusion: Fetal IVST was notably higher in uncontrolled diabetic mothers. There is a strong association between OGTT results and IVST. M-mode measurement of IVST is simpler than fetal echocardiography and can be included in routine third-trimester scans for diabetic mothers to detect early signs of hypertrophic cardiomyopathy.

1. Introduction

When glucose intolerance increases suddenly during pregnancy, it is called gestational diabetes mellitus (GDM).This definition covers the usage of insulin in therapy, as well as whether the disease continues beyond pregnancy or only diet adjustment. After a population screening for pregnant women with hyperglycemia, it is diagnosed [1,2].

The prevalence of GDM in India is 10.0%–14.3%, which is significantly higher than in the population of Western countries. Type 2 diabetes mellitus and insulin resistance rates in the population of each nation are followed by GDM. [3]. Therefore, it is anticipated that the incidence of GDM in India will rise to 20.0% or one in every five pregnant women. With the increasing incidence and complications of GDM, the whole health system will be facing even more dire consequences. Complications such as postpartum haemorrhage, caesarean sections, and infections are more prevalent among mothers who have been diagnosed with gestational diabetes mellitus (GDM). Newborns may experience birth trauma, congenital malformations, breathing difficulties, and problems regulating their blood sugar. The offspring of moms with unregulated diabetes at a fourfold increased risk of developing adult-onset diabetes and have worse long-term outcomes [4].

Poor glycemic control during pregnancy increases preterm births eight-fold, congenital abnormalities four to eight-fold, and perinatal mortality six-fold compared to the general population [5].Fetal difficulties associated with diabetes during pregnancy include heart disease, CNS disorders (such as spina bifida and anencephaly), genitourinary disorders, limb defects, excessive foetal development (macrosomia), and foetal growth retardation [6].Babies born to mothers with diabetes are at an increased risk of developing congenital health issues, with a preponderance of congenital cardiac problems ranging from 2.5% to 12.0%. [7].Hypoplastic left heart syndrome, transposition of the major arteries, truncus arteriosus, double outlet right ventricle and ventricular

septal defect are among the congenital cardiac issues that are observed in children of diabetic mothers. [8].While respiratory issues are common in these newborns, it is important to distinguish them from cardiovascular issues, which include hypertrophic cardiomyopathy, congenital heart abnormalities, and cardiovascular maladaptation to extrauterine life [9].Hypertrophic cardiomyopathy, a condition characterised by the enlargement of the interventricular septum, is recognised as a risk factor for infants born to maternal diabetics. This illness often shows no symptoms while the foetus is still developing, and it may only cause congestive heart failure in the first few hours after birth.

The impact on foetal metabolic status and foetal cardiovascular development depends critically on the onset and severity of maternal diabetes. First-trimester hyperglycemia in pre-gestational diabetes hurts foetal organogenesis and neural crest migration, which can lead to typical conotruncal heart irregularities. The distended foetal cardiac interventricular septums increase the risk of myocardial hypertrophy and diastolic abnormalities in foetuses with GDM. Pregnant women are particularly vulnerable to this during their second and third trimesters [10].A diabetic mother gives birth to 40.0% of infants with hypertrophic cardiomyopathy, 5.0% of which are symptomatic [11].There may be a metabolic condition worsening or a newborn hyperinsulinemia that increases insulin receptor expression and affinity, resulting in a proliferation of cardiac myocytes.

The anterior leaflet of the mitral valve contacts the interventricular septum during systole, resulting in a blockage of the left ventricle's outflow tract (LVOT). A hypertrophic cardiomyopathy is defined by an increase in left ventricular mass and contractile strength. The degree of septal hypertrophy directly correlates with reduced cardiac output because of a smaller stroke volume. This disproportionally thickened septum and asymmetric septal expansion are the anabolic outcomes of foetal hyperinsulinemia during the third trimester, which was sparked by maternal hyperglycemia. These changes are more apparent and simpler to identify in fetuses with asymmetrical septal hypertrophy. Fetuses with asymmetrical septal hypertrophy exhibit a substantial increase in interventricular septal thickness between 32 and 35 weeks of gestation when contrasted with those without. [12,13].Additionally, idiopathic respiratory distress syndrome and chronic pulmonary hypertension are relevant in third-trimester diabetic moms' babies who have asymmetrical septal hypertrophy. Thus, the purpose of our research is to ascertain how interventricular septal thickness is impacted by gestational diabetes mellitus.

2. Material and Methods

A two-month cross-sectional investigation was conducted in the Radiology Department of Sharda Hospital from April 2024 to June 2024, with an institutional ethical clearance number of SU/SMS&R/76-A/2024/82. A total of 90 consenting antenatal women of GA between 28 to 35 weeks were selected. 45 of these patients belonged to a major group of GA of 28 weeks 0 days to 32 weeks 0 days and the other 45 belonged to a study group of 32 weeks 1 day to 35 weeks 0 days. OGTT level was recorded at their first visit in the third trimester along with follow-up OGTT levels (after 2 weeks) to label them as non-diabetic (Subgroup A), controlled diabetic (Subgroup B) or uncontrolled diabetic (Subgroup C) (3 sub-groups). The normal OGTT level according to our institutional protocol was considered as 140 mg/dL. Fetal Interventricular septal thickness (IVST) measurements were obtained for all of them by M-mode in diastole. A three-time IVST measurement was conducted, and an average value was calculated, which was used as the basis of further analysis. The M-MODE acquisition of IVST was performed using curvilinear probes of Philips EPIQ 7G, Samsung SONOACER7 and Siemens ACUSON NX3.

Inclusion criteria: In this investigation, all consenting non-diabetic and diabetic pregnant women in their third trimester, with a gestational age ranging from 28 weeks 0 days to 35 weeks 0 days, recent reports of OGTT with follow-up levels, and a singleton pregnancy were included.

Exclusion criteria: Multiple Gestation, pregnant females with other co-morbidities, and diagnosed case of congenital anomaly were excluded.

Statistical Analysis:

SPSS software (version 23.0, SPSS Inc., Chicago, IL, USA) was employed to conduct data analysis. Continuous data were expressed as mean ± standard deviation, while categorical data were presented as percentages and numbers. The means of continuous variables were compared using independent samples t-tests. Where applicable, the chi-square test was implemented to evaluate the characteristics of the groups. The relationships

between gestational age, OGTT and HbA1c with IVST were evaluated using Pearson's correlation coefficient. Statistical significance was defined as a p-value of less than 0.05.

3. Results

The study duration was 12 months; from November 2022 to November 2023. The two major groups and the three subgroups, A, B, and C, included all research participants. Subgroups A, B, and C were defined as thirty non-diabetic moms, thirty managed diabetic mothers, and thirty uncontrolled diabetes mothers, respectively. There's no statistically significant difference (p-values > 0.05) in age distribution between subgroups within each gestational age group [Table no 1].

Table no 1: Age Distribution of Study Participants

Gestational Age (Week)	Age (Years)	Subgroup A	Subgroup B	Subgroup C	P value
GA 28-31 (n=45)	≤25	4 (26.7%)	8 (53.3%)	4 (26.7%)	0.195
	26-30	10 (66.7%)	7 (46.7%)	8 (53.3%)	
	>30	1 (6.7%)	0 (0.0%)	3 (20.0%)	
GA 32-35 (n=45)	≤25	5 (33.3%)	7 (46.7%)	7 (46.7%)	0.936
	26-30	8 (53.3%)	8 (53.3%)	5 (33.3%)	
	>30	2 (13.3%)	0 (0.0%)	3 (20.0%)	

In women at a gestational age of 28-31 weeks, 8 (53.3%), 11 (73.3%), and 11 (73.3%) patients in groups A, B, and C, respectively, were first-time mothers. There was no significant difference in the parity distribution across the subgroups (P>0.05). Likewise, there was no significant difference in parity distribution among subgroups for women with gestational age (GA) of 32-35 weeks (P>0.05).4 (26.7%) patients in subgroup A, 3 (20.0%) in subgroup B, and 3 (20.0%) in subgroup C were at 28 weeks gestation for those with gestational age falling between 28 and 31 weeks. There was no significant difference in gestational age among subgroups (P>0.05) [Table no. 2].

Table No. 2: Distribution of gestational age of the studied subjects

		Subgroup A	Subgroup B	Subgroup C	P value
GA 28-31	28	4 (26.7%)	3 (20.0%)	3 (20.0%)	0.993
	29	3 (20.0%)	2 (13.3%)	3 (20.0%)	
	30	4 (26.7%)	5 (33.3%)	5 (33.3%)	
	31	4 (26.7%)	5 (33.3%)	4 (26.7%)	
GA 32-35	32	6 (40.0%)	5 (33.3%)	6 (40.0%)	0.838
	33	5 (33.3%)	4 (26.7%)	5 (33.3%)	
	34	3 (20.0%)	6 (40.0%)	3 (20.0%)	
	35	1 (6.7%)	0 (0.0%)	1 (6.7%)	

It was demonstrated that fetal interventricular septal thickness had notable variations among the three subgroups in both gestational age categories of 28-31 weeks (P<0.001) and 32-35 weeks (P<0.001). In particular, the majority of fetuses in subgroup A had a thickness between 3.6 and 4.5, whereas all fetuses in subgroup C had a thickness above 4.5, irrespective of gestational age [Table no.3].

Table No. 3: Distribution of fetal interventricular septal thickness of the studied subjects

	Fetal interventricular septal thickness (mm)	Subgroup A	Subgroup B	Subgroup C	P value
GA 28-31	≤3.5	4 (26.7%)	1 (6.7%)	0 (0.0%)	<0.001
	3.6-4.5	11 (73.3%)	14 (93.3%)	0 (0.0%)	
	>4.5	0 (0.0%)	0 (0.0%)	15 (100.0%)	
GA 32-35	≤3.5	0 (0.0%)	0 (0.0%)	0 (0.0%)	<0.001
	3.6-4.5	13 (86.7)	3 (20.0%)	0 (0.0%)	
	>4.5	2 (13.3%)	12 (80.0%)	15 (100.0%)	

There was a notable discrepancy between subgroup A and subgroups B and C (P<0.001) for individuals with gestational age ranging from 28-31 weeks, while there was no significant difference between subgroups B and C (P=0.340). In the same way, individuals with gestational age ranging from 32 to 35 weeks showed significant differences between subgroup A and subgroup C (P<0.001) as well as subgroup B (P=0.001), with no significant

difference between subgroups B and C (P=0.189) [Table no. 4].

Table No. 4: Comparison of Level of significance of inter-subgroup

	Subgroup of subjects	P value
GA 28-31	Subgroup A vs group B	0.340
	Subgroup A vs Group C	**<0.001**
	Subgroup B vs Group C	**<0.001**
GA 32-35	Subgroup A vs group B	**0.001**
	Subgroup A vs Group C	**<0.001**
	Subgroup B vs Group C	0.189

The average thickness of the fetal interventricular septum varied significantly within the three subgroups for both gestational age ranges of 28-31 weeks (P<0.001) and 32-35 weeks (P<0.001). Subgroup C consistently had the thickest interventricular septum compared to subgroups A and B in both gestational age groups[Table no. 5].

Table No. 5: Average fetal interventricular septal thickness across various gestational ages among study participants

	Subgroup A	Subgroup B	Subgroup C	P value
GA 28-31	3.76±0.23	4.00±0.28	5.83±0.64	**<0.001**
GA 32-35	4.25±0.29	4.75±0.43	6.84±0.34	**<0.001**

A strong association was found between fetal interventricular septal thickness and maternal gestational age, initial and repeat OGTT results, and HbA1c levels (P<0.001 for all). This indicates that as these maternal factors increased, the fetal interventricular septal thickness also increased. (Table no. 6).

Table No. 6: Pearson correlation between fetal interventricular septal thickness and maternal gestational age, OGTT, and HbA1c levels

	IVST	
	Pearson's Correlation Coefficient	**P value**
GA	0.301**	**0.004**
First OGTT	0.645**	**<0.001**
Follow up OGTT	0.792**	**<0.001**
HbA1c	0.738**	**<0.001**
**. Correlation is significant at the 0.01 level (2-tailed).		

4. Discussion

High-risk pregnancies, such as those involving diabetes mellitus and preeclampsia, can have adverse effects on the fetus's growth and development in gestation. These effects may include an increase or decrease in fetal weight and postnatal NICU hospitalisation. Doppler indices and IVS thickness will be more affectionate in the presence of more coupled risk factors, which will ultimately impact the foetal outcome. The interventricular septal thickness was measured in our study to evaluate hypertrophic cardiomyopathy, a condition that impacts neonates and fetuses born to mothers with diabetes. Another consequence of elevated maternal glucose levels in diabetes pregnancies is an increase in fetal weight.

In cases of gestational diabetes mellitus (GDM), serial blood glucose and HbA1c level monitoring are often used to assess glycemic management. Only one pregnant participant in the current study had increased HbA1c values, indicating that HbA1c may not be a reliable indication of the metabolic state of the mother and foetus. However, in GDM pregnancies, foetal IVST was much greater. This is due to the fact that hyperinsulinemia has an anabolic effect on the foetus and consistently indicates the foetal metabolic status in the early third trimester. Consequently, it is capable of accurately predicting the onset of complications in GDM pregnancies. The purpose of this investigation was to contrast the interventricular septal thickness of the foetal heart between women who were diabetic and were under control for their condition, and those who were not.

A total of 90 consenting study subjects within 28 – 35-week gestational age were enrolled in this study and divided into 2 main groups and 3subgroups named Subgroup A, subgroup B and Subgroup C. Subgroup A consisted of 30 non-diabetic mothers, subgroup B of 30 controlled diabetic mothers, and subgroup C of 30 uncontrolled diabetic mothers. According to a similar study by Ghuman et al., among 70 pregnant women at

gestational weeks 24 to 32, 35 were affected by GDM and 35 were healthy controls [14].

The average age of patients in this study was 26.41±3.18 years, a value that was consistent across all subgroups. Most cases fell within the age range of 26 to 30 years across all groups ($p>0.05$). Our findings were in accordance with the findings of Rahman Y et alwho observed that almost half of the 80 participants (47.9%) belonged to group A (non-diabetic) with an age of ≤25 years, 44 (52.4%) to group B (managed diabetics) with an age of 26–30 years, and 44 (53.0%) to group C (uncontrolled diabetics) with an age of 26–30years. A statistically insignificant difference in the mean age of the groups was observed. ($p > 0.05$) [15].Previous studies reported similar age ranges for diabetic and non-diabetic participants as conducted by Nashaat et al., and Patchakapat et al. The findings of the current study align with these observations [16,17].

Within the group range of 32 to 35 weeks GA, nearly one-third of the participants in this series were found to be 32 weeks in group A (40.0%), 33.3% in groupB, and 40.0% in groupC. Rahman et al. conducted a study that similarly revealed no significant differences in gestational age among the three groups. [15]. Similarly, Zielinsky P et al showed at the time of assessment, the non-diabetic group's mean gestational age ranged from 25 to 36 weeks, the managed diabetic group's from 23 to 33 weeks, and the uncontrolled diabetes group's from 24-39 weeks and average gestational age was 30.6weeks [18]. Another study by Patchakapat L et aldiscovered that the mean gestational age ranged from 32 to 35 weeks, closely matching the findings of the current study, at 33.24±0.99 weeks [17].

In our study, the mean IVST amongst the nondiabetic pregnant females in GA 28-32 weeks was 3.76±0.23mm. Amongst the controlled & uncontrolled diabetics, it was 4.00±0.28mm & 5.83±0.64mm respectively. The mean IVST amongst nondiabetic pregnant females in GA 32 weeks 1 day-35 weeks was 4.25±0.29mm. Amongst the controlled & uncontrolled diabetics, it was 4.75±0.43mm & 6.84±0.34mm respectively [Figure 5]. The mean fetal IVST was significantly different between the groups, with subgroups non-diabetic & controlled diabetics having similar thicknesses & no statistical significance. While the sub-group uncontrolled diabetics had a significantly larger IVST amongst both the GA groups. Our results mirrored those of Rahman et al. in terms of fetal interventricular septal thickness (FIVST). In our study, similar proportions of participants in each group had FIVST measurements within the expected range (Group A), slightly exceeding it (Group B), and significantly exceeding it (Group C). Notably, the mean FIVST in Groups A and B did not differ significantly, but Group C exhibited a statistically significant increase compared to the other groups [15].In comparison to the non-diabetic and controlled diabetic groups, our findings regarding foetal interventricular septal thickness (IVS) were consistent with those of Rahman et al., who observed a substantial increase in IVS thickness in the uncontrolled diabetic group. It is important to note that the IVS in the non-diabetic and controlled diabetic groups did not exhibit a statistically significant difference, which is consistent with our study. [15].Nashaat EH, and Mansour GMin their study stated that higher mean interventricular septal thickness in 8 cases than in total cases of the nondiabetic group [16]. In their previous study, Gandhi JA et al. investigated the thickness of the foetal interventricular septum at 32 weeks. They found that group C had a substantially higher thickness (6.94±0.19 mm) than groups A (3.44±0.22 mm) and B (3.91±0.11 mm). This trend of a larger thickness in group C was observed at every gestational week studied [19].Our findings align with those reported in a prior Indian study by Garg et al., who observed comparable IVST measurements. Their study indicated that uncontrolled GDM resulted in higher IVST compared to both managed GDM and normal pregnancies [20].Supporting our findings, Russel et al. also observed increased fetal interventricular septal thickness and wall thickness in pregnancies with GDM compared to controls [21].Consistent with our observations, In addition, Ghuman et al. described a thicker foetal interventricular septum in the GDM group than in the control group. [14]. Building on prior research, Miranda et al. observed a similar trend: fetuses of diabetic mothers exhibited increased interventricular septal thickness compared to controls [22]. A study by Garcia-Flores et al investigated the fetal interventricular septal thickness in controlled gestational diabetes (excluding cases with HbA1c > 6.5%) compared to a control group. Interestingly, they found a significantly increased septal thickness in the diabetic group ($p < 0.001$) despite controlling for HbA1c levels [23].Prefumo et al. documented instances of significant foetal cardiac hypertrophy in foetuses of diabetic mothers, which was associated with signs of myocardial insufficiency.[24]. Our results indicate a potential correlation between septal hypertrophy and other complications associated with gestational diabetes, including hormonal imbalances or altered nutrient transfer through the placenta. Studies have shown a correlation between GDM and increased fetal ventricular septal thickness, particularly during the later stages of pregnancy as conducted by Russell et al [21].Additionally, Ghandi et al found that neonates of diabetic mothers were more likely to suffer septal hypertrophy [25].Research by Gordon EE et al. suggests that even brief periods of high blood sugar (hyperglycemia) during pregnancy can

lead to thickening of the wall separating the heart's lower chambers (ventricular septal hypertrophy) in newborns, including those born to mothers without diabetes [26].

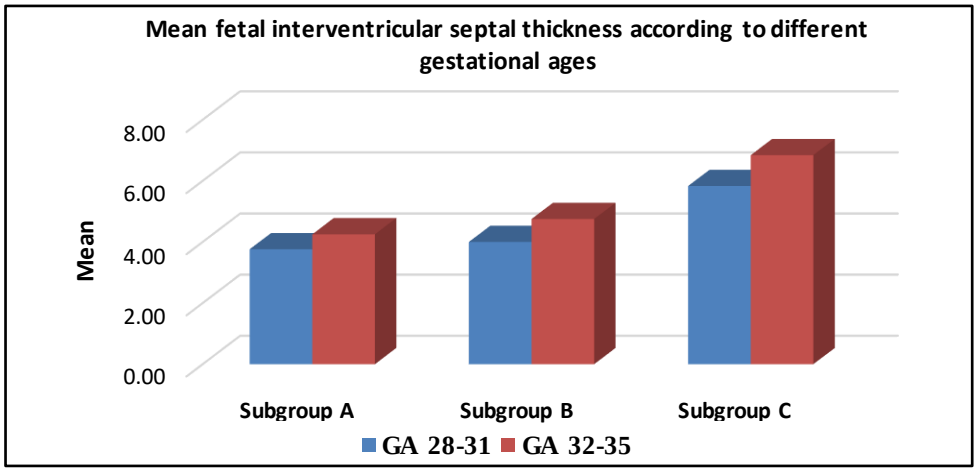

Figure 2: Mean fetal interventricular septal thickness according to different gestational ages

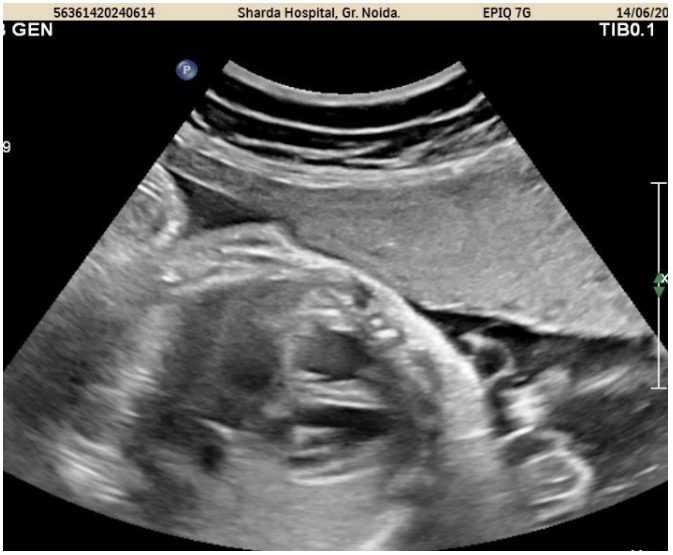

Figure 3(a) Illustrates lateral four chamber view of the fetal heart on grey scale ultrasound highlighting the interventricular septum (represents the interventricular septum).

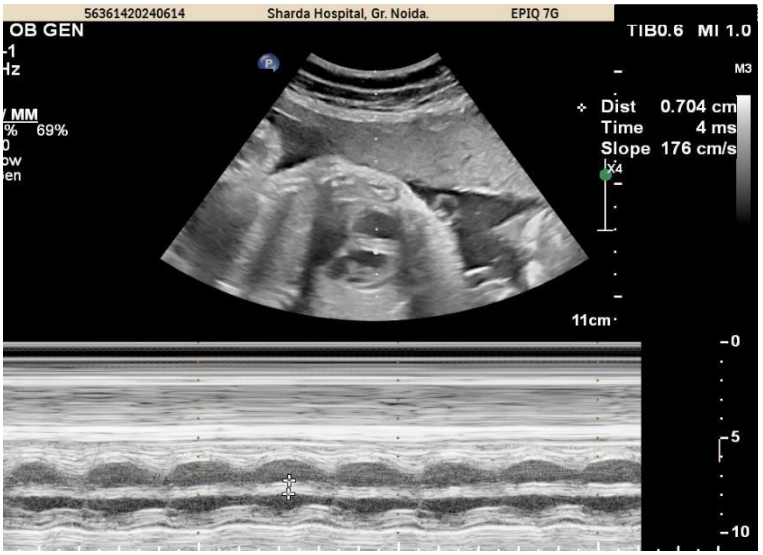

Figure 3 (b) demonstrates M mode acquisition of the fetal IVST. "The measurements were taken

perpendicular to the septum in the middle of its length in the lateral four chamber view".

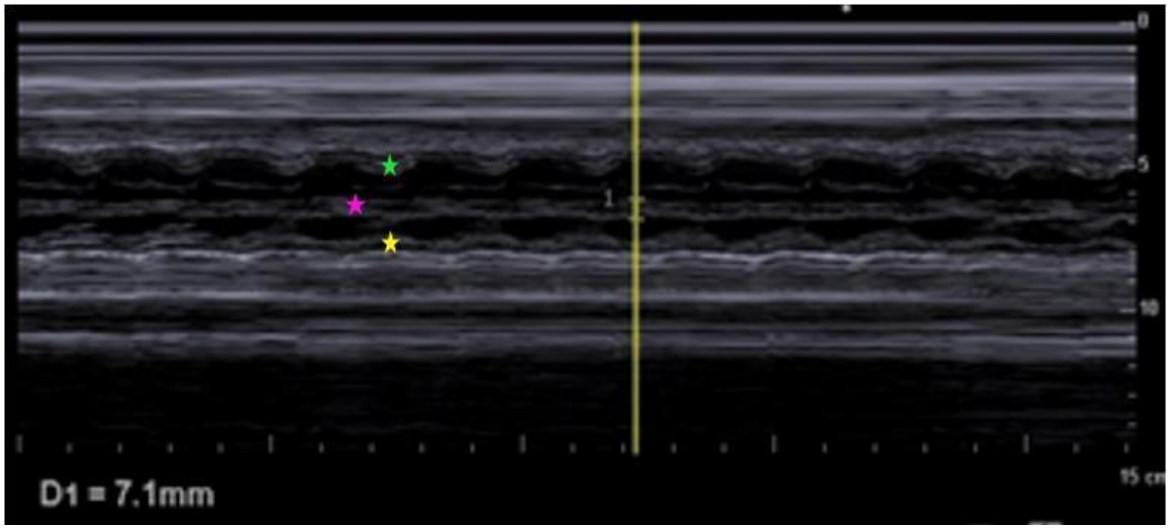

Figure 4: The measurements for IVST were taken perpendicular to the septum in the middle of its length in the lateral four chamber view. ★ represents Ventricular wall near the Probe. ★ represents Interventricular Septum with a thickness of approximately 7.1 mm. ★ represents Ventricular wall away from the probe.

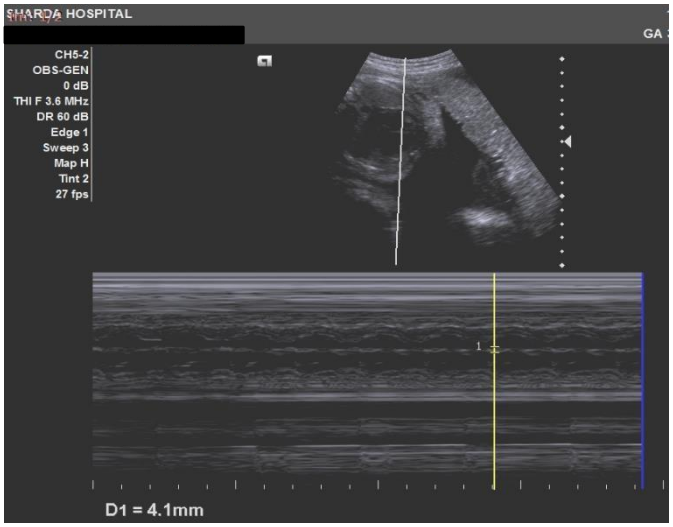

Figure 5. IVST in non-diabetic mother with GAof 33 weeks 1 day

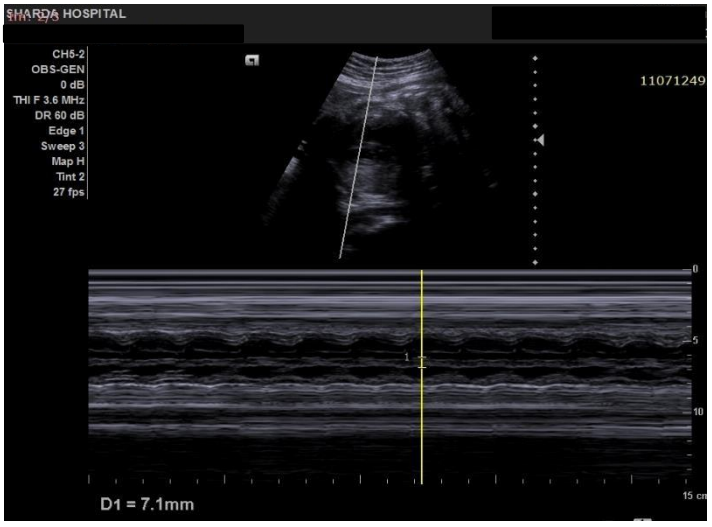

Figure 6. Un-controlled diabetic mother of GA 33 weeks 6 days

Pregnant women with diabetes carry a higher risk of hypertrophic cardiomyopathy and congenital heart disease. Particularly, in around 40% of foetuses from pregnant women with diabetes, myocardial hypertrophy was noted, with the interventricular septum (IVS) being the most impacted cardiac component [27].Increased ventricular wall thickness along with a smaller ventricular chamber, and decreased ventricular filling, which impairs diastolic ventricular function, and maybe lowers ventricular systolic performance are the hallmarks of hypertrophic cardiomyopathy. Echocardiograms typically reveal several characteristic findings in this condition: small heart chambers, abnormally forceful and thickened heart muscle (hypercontractile and thicker myocardium), thickening of the septum (septal hypertrophy) that's more pronounced than the surrounding heart wall (ventricular free walls), and a fluttering movement of the mitral valve forwards during contraction (anterior systolic motion of the mitral valve) which narrows the outflow pathway of the left ventricle (left ventricular outflow tract blockage) [10].

In this study, Pearson Correlation between fetal IVST and gestational age, OGTT levels and HbA1c showed a positive significant association($p<0.05$). According to Ali Hasan et al., the best assessment was observed in the late third trimester, when DM and IVS thickness were substantially correlated. [28].In contrast to our study, in non-diabetic patients, Rahman et al. observed a faint positive correlation between gestational age and foetal septal thickness. This discrepancy could be attributed to methodological variations, such as sample size differences, between the two studies [15].In a separate study, Patchakapat et al. investigated the relationship between interventricular septal thickness at the end of diastole (IVSd) and end of systole (IVSs) and gestational age. They reported correlation coefficients of 0.11 and 0.12, respectively [17].Ovesen P et al[29],investigated, using a cohort study, the impact of GDM on maternal and foetal outcomes. Preeclampsia, shoulder dystocia and scheduled or emergency caesarean sections were more prevalent among women with GDM. Thrombosis was more prevalent among patients with GDM. The probability of giving birth to a macrosomic neonate was higher among mothers with gestational diabetes mellitus. A modest Apgar score increased in the GDM.

This research's strength was that inter-observer bias was removed by employing a prospective design with a single observer. The research was primarily constrained by its limited sample size and the fact that it was conducted at a single centre. More studies in multi-institutional settings and with larger sample sizes are recommended to verify the accuracy. Additionally, all the individuals involved in this research were Indian females, and further confirmation is required to establish if the results are applicable to other racial backgrounds. In the third trimester, a regular scan may involve measuring interventricular septal thickness with an M-mode ultrasound.

5. Conclusion

Our study found that fetal interventricular septal thickness (IVST) was highest in mothers with uncontrolled diabetes, followed by mothers with controlled diabetes and then the non-diabetic group. The results of the Oral Glucose Tolerance Test (OGTT) and IVST exhibited a positive correlation, indicating a potential connection between maternal blood sugar levels and foetal cardiac development. So, we can conclude that increased IVST is directly related to poor glycemic control. Interventricular septal thickness calculation is fairly straightforward in M mode in comparison to Fetal Echocardiography. Thus, IVST by M-mode can be incorporated in routine Third-trimester scanning specially in diabetic mothers to pick up early changes of hypertrophic cardiomyopathy.

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