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Original Article

Radiology Section

Foetal Modified Myocardial Performance Index as a Predictor of Pregnancy Outcome in Gestational Diabetic Mothers: A Prospective Observational Study

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ABSTRACT

Introduction: Foetuses of mothers with Gestational Diabetes Mellitus (GDM) are at increased risk for cardiac complications even with metabolic control. Conventional Doppler methods often fail to detect early cardiac dysfunction in these cases. The Modified Myocardial Performance Index (Mod-MPI) offers a sensitive and non-invasive tool for early detection of foetal cardiac impairment in GDM pregnancies.

Aim: To assess foetal cardiac function using Mod-MPI by doppler in gestational diabetic mothers in early third trimester (28-32 weeks) and to evaluate its utility in prediction of perinatal outcome.

Materials and Methods: The present prospective observational study was conducted at VMMC and Safdarjung Hospital, New Delhi, India, from November 2017 to November 2018. A total of 30 singleton pregnant females in the third trimester (28-32 weeks) with a known history of GDM and 30 singleton pregnant females in the third trimester with no history of GDM were included. Patients with multiple pregnancy intrauterine growth retardation, Pre GDM, congenital anomalies, history of cardiac disease or hypertension were excluded from the study. Using doppler ultrasonography, the Mod-MPI was calculated in the foetal left ventricle. Multiple statistical tests and Receiver Operating Characteristic (ROC) analysis was used to determine the optimal Mod-MPI cut-off for predicting adverse foetal outcomes. A p-value <0.05 was considered statistically significant.

Results: The pregnant females with GDM had significantly higher mean MPI (0.67±0.14) compared to those females without GDM (0.47±0.08). The mean age in the cases was 26.77±3.45, and in the controls, it was 26.87±3.7 years. Abnormal outcomes were recorded in 9 of 30 foetuses of gestational diabetic mothers, and these foetuses had significantly higher MPI measurements (0.85±0.06), compared to the 21 GDM foetuses who had normal Mod-MPI (0.6±0.09) values without any adverse outcome. The MPI served as an excellent predictor of adverse outcomes in GDM foetuses with a total area under the ROC curve being 0.98. Three abnormal outcomes were recorded in the control group, including Apgar <7, stillbirth, and Intensive Care Unit (ICU) admission.

Conclusion: Mod-MPI has the potential to predict adverse pregnancy outcome and improve foetal surveillance in gestational diabetes.

Keywords: Abnormal outcome, Cardiac functional assessment, Doppler parameters, Isovolumetric contraction time, Isovolumetric relaxation time

INTRODUCTION

The GDM is defined as glucose intolerance first recognised during pregnancy, with its prevalence rising globally [1]. India has a notably high estimated GDM prevalence of 27.5% [1]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommend diagnosing GDM using a 75g 2-hour Oral Glucose Tolerance Test (OGTT) with a plasma glucose level ≥140 mg/dL [1].

Infants born to mothers with GDM are at increased risk of respiratory distress syndrome, transient tachypnoea of the newborn, acute pulmonary hypertension and myocardial hypertrophy which preferentially affects the interventricular septum [2]. Elevated Glycated Haemoglobin (HbA1c) is linked to congenital malformations, and despite metabolic control, systolic cardiac function may still be impaired. Late-gestation hyperglycaemia increases the risk of foetal macrosomia, hypoxia, polycythemia, and cardiomegaly with outflow tract obstruction [3,4].

Doppler-based foetal monitoring is insufficient for most GDM cases as they track mainly placental insufficiency, necessitating better assessment methods [5,6]. The MPI, introduced by Tei C et al., in 1996, evaluates global heart function by measuring Isovolumetric Contraction Time (ICT), Isovolumetric Relaxation Time (IRT), and Ejection Time (ET) {(MPI=(ICT+IRT)/ET)} [7-9]. The Mod-MPI improves accuracy by incorporating Doppler echoes from the Mitral Valves (MV) and Aortic Valves (AV) to measure different time periods for MPI calculation [10,11].

Modified MPI is particularly useful in foetal assessments, as it is independent of heart rate, blood pressure, and ventricular shape. It correlates well with other measures of left ventricular function and is easily incorporated into routine ultrasound examinations, making it a valuable tool for detecting early cardiac dysfunction in GDM-affected pregnancies [12].

The existing studies also prove the association between increased values of Mod-MPI and the complication rate in gestational diabetes, but none have been conducted in the Indian population. Moreover, most of the studies put more emphasis on pre-GDM rather than GDM [5,6]. The present study is unique in that it exclusively included all GDM in their 3rd trimesters who are controlled on diet, and it emphasised the value of the Mod-MPI in the Indian population in a busy tertiary care hospital. The study aimed to evaluate the role of the foetal Mod-MPI in predicting pregnancy outcomes.

MATERIALS AND METHODS

The present prospective observational study was conducted in the Department of Radiodiagnosis in collaboration with Obstetrics and Gynaecology and Paediatrics at VMMC and Safdarjung Hospital,

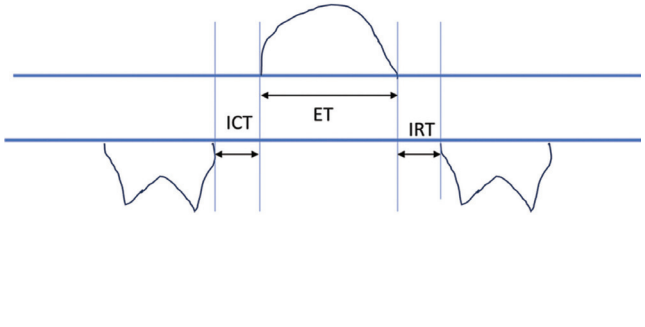
New Delhi, India, from November 2017 to November 2018. IEC approval was obtained. (IEC approval number IEC/VMMC/SJH/Thesis/October/2017-197). It included 30 gestational diabetic mothers controlled on diet and 30 healthy singleton pregnant women in their third trimester (≥28 weeks). The sample size of 60 (30 cases and 30 controls) was based on the expected number of eligible patients presenting during the study period.

GDM was defined as a plasma glucose value of ≥140 mg/dL after a 75 g 2-h OGTT [1].

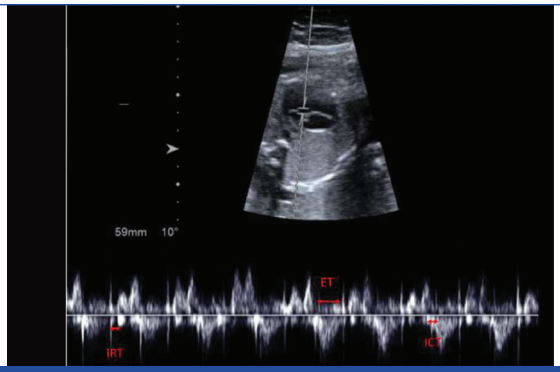
Inclusion and Exclusion criteria: Inclusion criteria for cases were gestational diabetic women (plasma glucose value of ≥140 mg/dL after a 75 g 2-h OGTT) in the third trimester (≥28 weeks). Inclusion criteria for controls were healthy singleton pregnant women in their third trimester (≥28 weeks). Exclusion criteria included multiple pregnancies, uncertain gestational age, cardiac disease, hypertension, obstetric haemorrhage, intrauterine growth restriction, congenital anomalies, abnormal amniotic fluid levels, and prior antenatal steroid use.

Study Procedure

Clinical assessment involved a detailed clinical history, general and abdominal examinations, and laboratory tests {Fasting Blood Sugar (FBS), 2 hPP, OGTT, HbA1c}. After undergoing laboratory investigations and giving informed consent, all 60 patients were subjected to sonography. Foetal cardiac function was assessed using doppler ultrasound (Philips iU22, 2-5 MHz transducer), measuring the Mod-MPI in the foetal left ventricle. Patients were placed in the supine position, and a cross-sectional image of the foetal thorax at the level of the 4-chamber view with an apical projection of the heart was obtained. The MPI was calculated in the foetal left ventricle. The doppler sample was opened to 3 mm and placed over the internal leaflet of the Mitral Valve (MV). In this location, owing to closeness to Aortic Valve (AV), the opening and closing AV clicks were registered. The angle of insonation was <30 degrees. E/A waveform reflecting ventricular filling was displayed as positive flow. The doppler gain was lowered as far as possible to clearly visualise the echoes corresponding to the opening and closing clicks of the two valves at the beginning and at the end of the MV and aortic waveforms. Measurement of the time intervals at the peak of the valve clicks was used. The doppler sweep velocity was set at 5 cm/sec and wall motion filter at 300Hz. The three time periods were measured as follows: ICT from beginning of MV closure to AV opening; ET from AV opening to closure; IRT from AV closure to MV opening. Mod-MPI was calculated as (ICT+IRT)/ET, with standardised protocols ensuring accuracy. A diagrammatic description of the components of the Mod-MPI is shown in [Table/Fig-1] and [Table/Fig-2] shows how the Mod-MPI was calculated using the doppler. Adverse pregnancy outcome was recorded in the form of stillbirth, neonatal death, five minutes Apgar score <7, admission to the neonatal ICU, respiratory distress syndrome, and hypoglycaemia.



[Table/Fig-1]: Shows diagrammatic description of the components of MPI. ICT: Isovolumetric contraction time; IRT: Isovolumetric relaxation time; ET: Ejection time.



[Table/Fig-2]: MPI=ICT+IRT/ET. ICT: Isovolumetric contraction time; IRT: Isovolumetric relaxation time; ET: Ejection time

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean±SD and median. Normality of data was tested by the Kolmogorov-Smirnov test. If the normality was rejected, then non parametric test was used. Continous variables were compared using unpaired t-test/Mann-Whitney test (when the data sets were not normally distributed) between the two groups. Categorical variables were compared using Chi-square test. The ROC curve was used to find out cut-off point of MPI for predicting adverse foetal outcome. Diagnostic test was used to find out sensitivity, specificity, Positive Predictive value (PPV) and Negative Predictive Value (NPV). A p-value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULTS

The majority of the patients belonged to the >25 years' age group (n=43), comprising of 21 cases and 22 controls followed by the 18-25 years age group (n=17), comprising of nine cases and eight controls. The mean age in the cases was 26.77±3.45 and in controls was 26.87±3.7. Cephalic presentation was the commonest presentation in the current study (n=42). The mean gestational age at the time of delivery was 38±2 weeks. Both groups were almost similar in terms of gravidity and parity. Mean gravida of the cases was 2.3 and of controls were 2.2. Mean parity of cases was 0.92 and of controls was 0.86. The BMI of the study group was 33.7±5.6 and of the control group was 27.3±4.2.

A total of nine of the 30 foetuses in the GDM group had at least one complication. There was an ICU admission and a stillbirth in the control population [Table/Fig-3].

Adverse outcomes	GDM group (n=30)	Controls (n=30)
Apgar <7	8	2
Stillbirth	1	1
ICU admission	4	1
RDS	3	0
Hypoglycaemia	3	0
Neonatal death	0	0
Total adverse outcomes	9	3
Normal outcome	21	27

[Table/Fig-3]: Shows adverse outcomes in cases and controls.

There was one case of stillbirth in the GDM population. The patient presented in the 30th week of gestation with poorly controlled diabetes and polyhydramnios; however, the doppler parameters were normal, and the Mod-MPI was raised (0.73). The patient was admitted, and close monitoring was done when late decelerations were noted in the CTG. A caesarean section was done, and a stillborn was delivered.

The mean value of Mod-MPI was 0.67±0.14 in the gestational diabetic cases and 0.47±0.08 in controls, and was significantly

higher in GDM cases than in controls [Table/Fig-4a]. In cases with adverse outcomes, the mean value of Mod-MPI was 0.85±0.06, and in cases without adverse outcome, the mean value of Mod-MPI was 0.6±0.09, and it was statistically significant [Table/Fig-4b].

Parameters	Case	Control	p-value
IRT			
Sample size	30	30	<0.0001
Mean±St.dev	53.3±8.33	42.2±4.77	
Median	52	41.5	
Min - Max	40-76	37-56	
Interquartile range	50-58	38 - 44	
ET			
Sample size	30	30	<0.0001
Mean±St.dev	135.5±17.27	166.27±11.31	
Median	136	170	
Min-Max	96-169	125-176	
Interquartile range	125-148	166-172	
MPI			
Sample size	30	30	<0.0001
Mean±St.dev	0.67±0.14	0.47±0.08	
Median	0.63	0.44	
Min-Max	0.44-0.93	0.39-0.65	
Interquartile range	0.560-0.790	0.420-0.480	

[Table/Fig-4a]: Shows a comparison of IRT, ET and MPI between cases and controls. t-test was used

Parameters	Adverse outcome absent	Adverse outcome present	p-value
IRT			
Sample size	21	9	0.002
Mean±St.dev	50.38±6.22	60.11±8.95	
Median	50	58	
Min-Max	40-64	50-76	
Interquartile range	45.750-52.500	52-64.500	
ET			
Sample size	21	9	0.006
Mean±St.dev	140.9±14.01	122.89±18.3	
Median	140	120	
Min-Max	112-169	96-164	
Interquartile range	134.500-48.500	115-128	
MPI			
Sample size	21	9	<0.001
Mean±St.dev	0.6±0.09	0.85±0.06	
Median	0.6	0.84	
Min-Max	0.44-0.79	0.73-0.93	
Interquartile range	0.545-0.640	0.820-0.903	

[Table/Fig-4b]: Shows comparison of IRT, ET and Mod-MPI between cases with normal outcome and cases with adverse outcome. Mann-Whitney test was used

In terms of actual Mod-MPI values, a cut-off of 0.67 was associated with a sensitivity of 100% and specificity was 90.5% as a predictor of adverse outcome in gestational diabetes [Table/Fig-5].

DISCUSSION

Foetal complications in gestational diabetes are not related to placental insufficiency but to foetal hyperinsulinism and the resultant abnormal metabolic milieu. The standard doppler parameters such as umbilical artery doppler, uterine artery doppler, middle cerebral artery doppler, ductus venosus evaluation are ineffective in detecting the effect of the abnormal metabolic milieu on the foetuses of the gestational diabetic mothers, as they are meant to detect the placental-mediated resistance [13].

The difference in MPI values in the current study and the rest of the studies [3,4] could be explained by the fact that the gestational age was slightly different in our study as compared to other studies, and also, since MPI is an operator-dependent parameter, there could be some interobserver variations. Bhorat I et al., used a mean gestation age of 34.16 weeks in controls and 34.19 weeks in the cases, and Balli S et al., did their study between 24-36 weeks of gestation [3,4].

The mean maternal age in the study done by Balli S et al., was 31.57±5.9 years in cases and 27.95±5.8 years in controls [4]. Bhorat I et al., did not make a mention of the maternal age taken in their study for assessing the role of MPI in gestational diabetes [3]. The difference in age in the present study is likely to be due to the varied customs and different lifestyle in the country where the study was conducted where the average age of marriage and pregnancy is lower. The investigators chose a population consisting of pregnant females with gestation between 28-32 weeks. They chose this period of gestation as during the early third trimester, Mod-MPI was seen to relate well with the abnormal pregnancy outcome.

Bhorat I et al., in women with severely impaired gestational glucose intolerance controlled on insulin showed that the mean MPI was 0.38 in controls and 0.59 in cases [3]. In the cases with adverse outcomes, the mean value of MPI was 0.62, and in the cases with normal outcomes, the mean value of MPI was 0.45. Ozturk M et al., used a cut-off of 0.41 to predict adverse perinatal outcomes in GDM patients [14]. Sanhal CY et al., did a similar study in 70 gestational age matched both pregestational and gestational diabetic women and according to this study, the foetal left ventricular MPI values were significantly higher in the diabetic group compared with the controls (0.56±0.09 vs 0.36±0.04) [15]. Balli S et al., in his study from 24-36 weeks of gestation mentioned that between 24 and 36 weeks, the value of MPI was significantly greater in gestational diabetic mothers (0.45±0.01) than in the controls (0.41±0.01) [4]. Figueroa H et al., mentioned that the value of MPI in controls was 0.371±0.044, in gestational diabetics was 0.418±0.063, and in pregestational diabetes was 0.451±0.072 [5].

There are a number of reasons for the association between an elevated Mod-MPI and the adverse outcome. The most important

Parameters	Area under the ROC Curve (AUC)	Standard error	95% Confidence interval	p-value	Cut-off	Sensitivity	Specificity
AFI	0.548	0.125	0.356 to 0.729	0.7043	>16	33.33	95.24
ICT	0.646	0.109	0.451 to 0.810	0.1835	>39	88.89	47.62
IRT	0.825	0.0786	0.644 to 0.939	<0.0001	>56	66.67	85.71
ET	0.828	0.102	0.647 to 0.940	0.0013	<128	88.89	80.95
MV-E	0.725	0.0983	0.532 to 0.871	0.0222	<34	100	52.38
MV-A	0.516	0.516	0.327 to 0.701	0.9105	>38	55.56	14.29
E/A	0.807	0.807	0.622 to 0.940	0.0014	<0.63	77.89	90.48
Mod-MPI	0.987	0.987	0.860 to 1.000	<0.0001	>0.67	100	90.48

[Table/Fig-5]: ROC analysis for the various parameters. Chi-square test was used.
Notes: pes of implan

is the progressive thickening of the foetal interventricular septum associated with a decrease in the ratio between the peak velocities during early passive ventricular filling and active atrial filling at the level of atrioventricular valves [3,4]. Diastolic dysfunction due to the impaired ventricular compliance is also reported in these foetuses as evidenced by decreased E/A ratio and prolongation of IRT in our study. The inferior vena cava in the foetuses of gestational diabetic mothers has also been reported to show increased preload index, which can lead to lower umbilical artery pH, higher haematocrit at birth, and increased neonatal morbidity [3]. The other reasons that can be considered are abnormal pulmonary systolic pressure, lactic acidosis in the absence of hypoxaemia [3].

The purpose of using cardiac functional assessment in gestational diabetes is that there are several alterations in the ventricular compliance in response to the abnormal metabolic milieu, and this could be the main mechanism leading to foetal compromise in gestational diabetes [15,16]. The traditional foetal monitoring parameters, such as doppler assessment of the umbilical artery, uterine artery, middle cerebral artery, and the ductus venosus, mainly detect and monitor the placental insufficiency rather than the abnormal metabolic milieu [16]. Also, in diabetic pregnancies, significant acidaemia and lactic acidosis can occur in the foetuses in the absence of hypoxaemia, which may render standard monitoring tools ineffective, necessitating the need for searching alternative monitoring tools to monitor diabetics [15-17].

The strengths of the present study were that Mod-MPI came out to be a significant predictor of the adverse outcome in gestational diabetic mothers. Since, it is a very convenient and easy to do technique if mastered, MPI has a good potential in becoming a monitoring tool to detect possible foetal deterioration in gestational diabetes and helping the clinicians to time the delivery for optimal outcome.

Limitation(s)

The drawbacks of the present study were the small number of subjects in the study and the control group. Mod-MPI requires a lot of experience and training to obtain a reliable result, and there can be a lot of interobserver variations, adding another limitation to this study.

CONCLUSION(S)

Foetal compromise remains a significant concern for Obstetricians, Neonatologists, mothers, and their families. The study findings demonstrate a significant association between an elevated MPI and adverse perinatal outcomes. Therefore, the Mod-MPI emerges as a promising and relatively novel marker for assessing perinatal outcomes in foetuses of gestational diabetic mothers.

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