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Original Article

Fetal Left Ventricle Modified Myocardial Performance Index: Defining Normal Values in the Third Trimester in Rural Central India

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Abstract

Introduction: Myocardial performance index (MPI) is an emerging non-invasive parameter for *in utero* monitoring of fetal well-being.

Purpose: The aim of this study was to determine normal values for fetal left ventricle (LV) modified MPI (Mod-MPI) in Indian population and to assess its relation to advancing gestation and fetal heart rate (FHR).

Materials and Methods: In this study, 60 normal pregnant women were included whose fetuses were having structurally normal hearts. Fetal echocardiography was done to measure the LV Mod-MPI. MPI was calculated after measuring various time intervals including isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT), and ejection time (ET), and the formula used for MPI calculation was ICT + IRT/ET. Further, linear regression analysis was done to find a correlation of MPI with the gestation age and FHR.

Results: The normal MPI in the third-trimester fetuses of the Indian population was 0.35 ± 0.03. The mean ICT was 31.40 ± 2.95 ms, mean IRT was 32.38 ± 3.42 ms, and mean ET was 174.83 ± 6.41 ms. The mean heart rate was 142 ± 6 bpm. The LV Mod-MPI was not significantly associated with either FHR or advancing gestation.

Conclusion: Fetal global cardiac function can be assessed by MPI. FHR, ventricular size, and geometry or image quality do not have any effect on MPI. MPI has a significantly important role in the monitoring of complicated pregnancies.

Key words: Fetal cardiac function, Left ventricle, Myocardial performance index

INTRODUCTION

A significant advancement is noted in fetal cardiology field in the past few decades. Initially, fetal echocardiography was used by Allan *et al.* for the systematic examination of the heart by fetal ultrasound including four-chamber view, outflow tracts, and promoted routine screening for fetal cardiac abnormalities.[1] Now, cardiac function, cardiac anatomy, and hemodynamic assessment can be done by echocardiography. Ventricular fractional shortening or ejection fraction can assess the systolic function.[2] Assessment of diastolic function can be done by pulsed Doppler of ventricular inflows, inferior vena cava, ductus venosus, or umbilical vein. However, these parameters are often a late marker of ventricular dysfunction.

Recently, the modified myocardial performance index (Mod-MPI) is now being used as a noninvasive pulsed wave Doppler-derived measure for the assessment of global myocardial function and important tool in the evaluating fetal cardiology.[3] Fetal cardiac systolic function in the form of the aortic ejection time (ET) and diastolic function in the form of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT)[3] can be simultaneously evaluated by Mod-MPI. The Mod-MPI is a potentially useful method of estimating fetal cardiac adaptive changes

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in complicated pregnancies such as intrauterine growth restriction,[4] maternal diabetes,[5-7] twin-twin transfusion syndrome (TTTS),[8] congenital heart malformations,[9] and preeclampsia.[10] MPI does not require anatomical imaging; it is independent of heart rate, blood pressure, and ventricular shape as it only requires time intervals.[11,12] MPI helps in identifying the high-risk population in various pregnancy-related complications and helps the stratifying the patients into high-risk and low-risk group and their subsequent management. Pulsed wave Doppler-derived MPI is widely used first in adults and then in the pediatric population[13-15] for the quantitative measurement of the global cardiac function.[16] Cardiac dysfunction in the subclinical phase can be diagnosed by MPI. However, it has limited use in cardiac assessment, and the main reason is lack of normal reference ranges and awareness regarding its role for detection of various fetal conditions. This study was done to determine the normal values for fetal left ventricular (LV) Mod-MPI in the third-trimester fetuses of the Indian population.

MATERIALS AND METHODS

Ethics Statement

All patients enrolled in this study were briefed about the nature, and the course of the study and informed consent in the regional language was taken from them.

Approval from the institutional ethics committee was sought before beginning the study.

Study Design

This was hospital-based, prospective, and diagnostic study.

Study Setting and Period

This study was conducted in ultrasound section of the department of radiodiagnosis from December 2015 to October 2017.

Sample Size

A total of 60 pregnant women with normal pregnancies served as the study group.

Subjects

All pregnant women who were referred to ultrasound section of the department of radiodiagnosis for their routine ultrasound scan at 28–40 weeks of gestation, willing to participate in the study and were having singleton pregnancy were included in the study. The women who were not willing to participate in the study, having multiple gestations, congenital heart disease, preeclampsia, diabetes mellitus, and intrauterine growth restriction were excluded from the study. In case of more than one examination of a fetus, results of the last examination were included from the study.

Equipment Used

Ultrasound examination was performed with a transabdominal 2.5–5 MHz curvilinear transducer and volume transducer on the ultrasonography machines available in the department (VolusonS6 WIPRO GE healthcare ultrasonography machines and Philips Affinity 70 machine).

Study Methodology

After taking the consent, cases were enrolled in the study. All obstetrics ultrasounds were done strictly following the guidelines under the PCPNDT act and after filling of form F (form for maintenance of record in respect of pregnant women by genetic clinic/ultrasound clinic/imaging center) and consent form.

A predesigned, validated, and pre-tested pro forma was used as a study tool to collect information such as name, age, the area of residence, and maternal history for any risk factors for congenital heart disease. Then, after the obstetric ultrasound, fetal echocardiography was done, and MPI was measured.

Technique[17,18]

The technique used to obtain the LV Mod-MPI was as described by Hernandez-Andrade *et al.* A four-chamber view of the heart with an apical projection of the heart was obtained. The transducer was slightly displaced in the cranial direction where the mitral and aortic valves were visible. Sample gate of about 3–4 mm was placed at a location to include both the lateral wall of ascending aorta and the internal leaflet of the mitral valve as shown in Figure 1. The gain was reduced so that noise and artifacts were reduced on US screen display. High wall motion filter was set to avoid recording slow blood movements. In Doppler settings, fast Doppler sweep velocity (15 cm/s) was used.

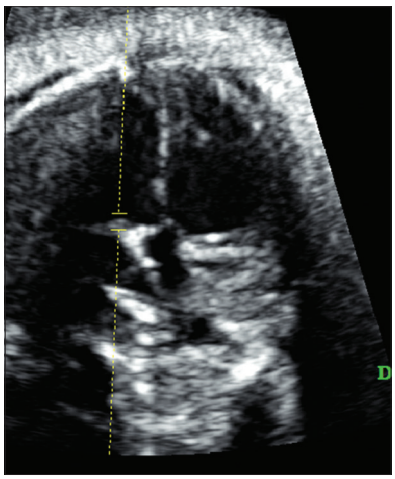

Figure 1: Positioning of the Doppler sample volume for acquisition of the myocardial performance index at the lateral wall of ascending aorta just below the aortic valve leaflet and above the mitral valve leaflet. Both atrioventricular and aortic valves should be visible in the section

The angle of insonation was kept <30°. The waveform was obtained, and the clear valve clicks corresponding to the opening and closing of the two valves were apparently imaged to correctly place the time cursors as shown in Figure 2. This estimation should be performed 3 times. Three time periods were estimated as follows: Isovolumetric contraction time (ICT) from the beginning of MV closure to AV opening clicks as shown in Figure 3; Ejection time (ET) from AV opening to AV closure click; Isovolumetric relaxation time (IRT) from AV closure to MV opening click as shown in Figure 3. The Mod-MPI = (ICT +IRT) /ET. For the purpose of the study, if days exceeded weeks by <4 days then the weeks of GA were rounded downward and when days exceeded weeks by ≥4 days then the weeks rounded upward.

Postnatal Follow-up

Postnatal follow-up outcomes were recorded. All neonates were evaluated by neonatologist at birth and till discharge from the hospital.

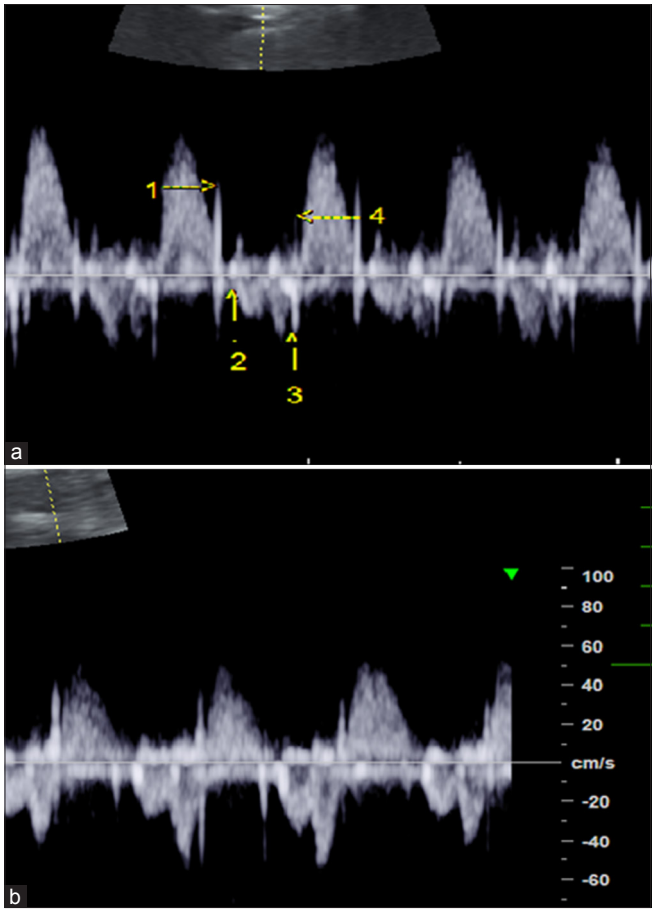

Figure 2: (a and b) The waveform used for the calculation of myocardial performance index and various clicks used for the time measurement. 1 is aortic valve closure click, 2 is mitral valve opening click, 3 is mitral valve closure click, and 4 is aortic valve opening click in figure 8(a)

Statistical Analysis

Data entry was done in the Microsoft Excel spreadsheet. Statistical analysis was done using descriptive and inferential statistics using Chi-square test, Student's unpaired *t*-test, one-way ANOVA, multiple comparison Tukey test, and software used in the analysis were SPSS 22.0 version and GraphPad Prism 6.0 version and $P < 0.05$ is considered as the level of statistical significance. The relationship of the MPI with gestational age and heart rate was measured by linear regression analysis.

RESULTS

A total of 60 pregnant women with single, normal healthy fetuses were enrolled in this study [Table 1].

Fetal ICT, IRT, ET, and fetal heart rate (FHR) were measured in all fetuses [Table 2]. Mean ICT was 31.40 ± 2.95 ms, mean IRT was 32.38 ± 3.42 ms, and mean ET was 174.83 ± 6.41 ms. The mean heart rate was 142 ± 6 bpm. Mean Mod-MPI was 0.35 ± 0.03.

The correlation coefficient analysis revealed no correlation between MPI and the gestational age ($r = 0.04$) [Table 3] and MPI and the FHR [Table 4].

DISCUSSION

Assessment of fetal cardiac function and to predict potential progression to dysfunction is still under evolution. Fetal cardiac dysfunction can be measured by the LV Mod-MPI and creates a viable and reproducible *in utero* fetal monitoring for the fetal well-being. MPI can detect

Table 1: Distribution of patients according to gestational age in the third trimester (28–40 weeks)

Number of patients	Mean gestational age (weeks)	Mean±MPI
60	35.8±1.54	0.35±0.03

Table 2: Comparison of fetal parameters and LV modified MPI parameters

Variable	Study group
Maternal mean age (years)	27.53±2.20
Gestational age (mean weeks)	35.8±1.54
EWF (g)	2721±509.26
AFI (cm)	11.06±3.01
Modified LV MPI	0.35±0.03
ICT (ms)	31.40±2.95
IRT (ms)	32.38±3.42
ET (ms)	174.83±6.41

EWF: Expected fetal weight, AFI: Amniotic fluid index, MPI: Myocardial performance index, ICT: Isovolumetric contraction time, IRT: Isovolumetric relaxation time, ET: Ejection time

the subclinical diastolic dysfunction,[19] and it could serve as a guide to clinicians to establish the timing of delivery and ultimately will reduce the perinatal morbidity and mortality. Increased MPI is highly sensitive and specific for the prediction of adverse perinatal outcome including stillbirth or neonatal death.[20,21,27] Mod-MPI has potential to improve fetal surveillance, and we can stratify the high-risk pregnancies into high-risk or low-risk pregnancies. IRT is the important parameter which becomes abnormal early in myocardial dysfunction mainly because of reduced calcium uptake.[22] Previously published reference values for MPI values varied from 0.22 to 0.53.

Multiple studies have been done to determine the normal values of MPI in the fetus [Table 5] and with varied results.

Table 3: No correlation between gestational age and Tei index

Gestational Parameters	Mean±SD	*n*	*r* value	*P* value
Gestational age	39.06±1.02	60	0.04	0.25, not significant
Tie index	0.35±0.015	60		

SD: Standard deviation

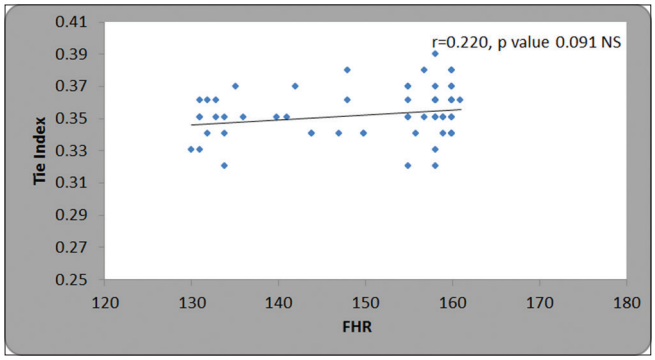

Table 4: No correlation between Tie index and FHR

Gestational Parameters	Mean±SD	*n*	*r* value	*P* value
Tie Index	150.15±11.03	60	0.220	0.091, not significant
FHR	0.35±0.01	60		

FHR: Fetal heart rate, SD: Standard deviation

Table 5: Comparison with the previous similar studies

Study	Year	Number of patients	Modified MPI
Tsutsumi *et al*.[3]	1999	135	0.43±0.03
Eidem *et al*.[23]	2001	125	0.36±0.06
Friedman *et al*.[24]	2003	74	0.53±0.13
Chen *et al*.[29]	2006	225	0.22±0.05
Hernandez-Andrade *et al*.[17]	2007	557	0.37±0.029
Ghawi *et al*.[25]	2013	420	0.464±0.08
Nair and Radhakrishnan[26]	2016	200	0.42±0.03
Present study	2017	60	0.35±0.03

Tsutsumi *et al*. were the first to use Tei index for the assessment of fetal global myocardial function. The LV MPI was significantly lower (0.43 ± 0.03) in the third trimester beyond 34 weeks of gestation as compared to the second-trimester fetuses between 18 and 26 weeks of gestation (0.62 ± 0.07).[3] The LV myocardial maturational changes significantly increased in the late gestation, and global ventricular function got affected by these maturational changes. This leads to the difference in MPI in the above-mentioned study. A similar decrease in MPI with advancing gestation was also noted by Chen *et al*.[29] In contrast to this, Friedman *et al*., Parasuraman *et al*.,[30] and Russel and McAuliffe[31] reported that the MPI values did not show any significant correlation with gestational age and heart rate.[24] Our study correlated well with the fact that the MPI has no correlation with either gestational age or heart rate. The technique for MPI measurement has been improved with time. Tsutsumi *et al*., in 1999, first reported the use of the MPI using two waveforms, and therefore, two cardiac cycles were used for measurements.[3] Then, further, Friedman *et al*. proposed a new position for the Doppler sample volume in 2003 and from which the LV MPI can be calculated from a single Doppler waveform.[24] Raboisson *et al*., in 2003, proposed that the Doppler click of the aortic valve opening be used as a landmark which helped to better estimate the time intervals of MPI calculation.[16] In 2005, Mod-MPI was introduced by Hernandez-Andrade *et al*. in which they used the beginning of opening and closing Doppler clicks of both the aortic and mitral valves as measurement landmarks for the different time periods.[22] Using this method, there was a significant reduction in the inter- and intra-observer variability, and thus, reproducibility of the index in fetal medicine was improved.

The clinical applications for MPI in early detection and counseling were investigated. Fetal cardiac dysfunction was assessed by MPI in a variety of pathological conditions including intrauterine growth restriction,[4] maternal diabetes,[5-7] TTTS,[8] congenital heart malformations,[9] preeclampsia,[10] and fetal inflammatory response syndrome in fetuses with preterm premature rupture of membranes[28] and MPI was significantly increased in the above-mentioned studies. Increased MPI is highly sensitive and specific for the prediction of adverse perinatal outcome including stillbirth or neonatal death.[20,21,27]

It is already reported that machine settings and technique used for MPI evaluation significantly affect the reproducibility, and it may account for the variation in the wide range of normal values. The accurate role of MPI values in complicated pregnancies is limited due to lack of universal normal reference ranges. To establish a universal reference range of MPI, large multicenter studies

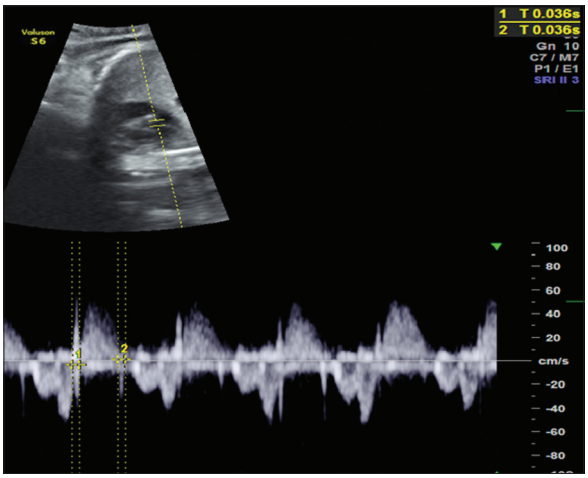

Figure 3: The measurement of isovolumetric contraction time (1) from the mitral valve closure click to the aortic valve opening click. Isovolumetric contraction time was measured 36 ms. Number 2 is showing isovolumetric relaxation time, measured 36 ms

are needed to measure the MPI using standardized machine settings and technique.

Limitation

The possibility of intraobserver errors from the study cannot be excluded as all the observations were made by a single operator.

CONCLUSION

The normal range of the LV Mod-MPI in normal fetuses of the Indian population was defined by our study. The LV MPI values appear to be independent of GA and FHR. MPI can be used as a screening/follow-up tool for global cardiac function in normal and complex fetal hearts. Subclinical fetal cardiac dysfunction can be measured by the LV Mod-MPI and creates a viable and reproducible *in utero* fetal monitoring for the fetal well-being. MPI should be considered as an adjuvant in the initial diagnosis in fetuses with complex heart diseases and their subsequent follow-up scans. Prospective studies are needed to further delineate these relations.

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