

# Evaluation of Foetal Modified Myocardial Performance Index as a Predictor of Perinatal Outcome in Intrauterine Growth Restriction Foetuses: A Prospective Cohort Study

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## ABSTRACT

**Introduction:** Functional cardiovascular assessment is gaining significance as a key tool in understanding foetal pathology. The foetal Modified Myocardial Performance Index (Mod-MPI) is a non invasive, pulsed-wave Doppler-derived measure of global cardiac function. Mod-MPI is independent of ventricular size, geometry and heart rate. Despite advances in the diagnosis and management of Intrauterine Growth-Restricted foetuses (IUGR), there remains a small proportion of cases that face severe adverse perinatal outcomes despite normal conventional Doppler studies. This highlights the need for new indices such as Mod-MPI for improved perinatal outcomes.

**Aim:** To assess foetal cardiac function using Mod-MPI in IUGR foetuses in the third trimester and to compare Mod-MPI values with those of normal controls.

**Materials and Methods:** The prospective cohort study was conducted in the Department of Radiology at Government Coimbatore Medical College Hospital, Coimbatore, Tamil Nadu, India, from May 2024 to December 2024. A total of 43 singleton pregnancies in the third trimester with IUGR (cases) and 43 gestational age-matched normal singleton pregnancies in the third trimester (controls) were included in the study and were

followed until delivery. The Mod-MPI was calculated in the foetal left ventricle by placing the Doppler sample in the internal leaflet of the mitral valve and estimating three time periods: Isovolumetric Contraction Time (ICT), Isovolumetric Relaxation Time (IRT) and Ejection Time (ET). The Mod-MPI was calculated as  $(ICT+IRT)/ET$ . Independent sample t-tests and Chi-squared tests were used for comparison between cases and controls.

**Results:** The mean Mod-MPI value in the control group was found to be 0.41, with a Standard Deviation (SD) of 0.05. In IUGR cases, the mean Mod-MPI value was found to be  $0.56 \pm 0.06$ . The p-value was  $<0.001$ . Based on the results, a value of 0.4950 was taken as a cut-off in the present study for the occurrence of adverse perinatal outcomes. Moreover, IUGR foetuses with higher left Mod-MPI values were associated with significantly worse perinatal outcomes and increased morbidity compared to the control group and IUGR foetuses with normal Mod-MPI values.

**Conclusion:** The Mod-MPI is a simple and sensitive parameter for early foetal cardiac adaptation and higher MPI values were significantly associated with adverse perinatal outcomes, even in the presence of normal conventional Doppler findings.

**Keywords:** Antenatal surveillance, Foetal cardiac function, Foetal doppler studies, Foetal echocardiography, Perinatal morbidity and mortality

## INTRODUCTION

Functional cardiovascular assessment is gaining significance as a key tool in understanding foetal pathology [1]. The foetal Modified Myocardial Performance Index (Mod-MPI) is a non invasive, pulsed-wave Doppler-derived measure of global cardiac function [2]. Mod-MPI is independent of ventricular size, geometry and heart rate [3]. Previous studies have revealed that Mod-MPI is affected even when the umbilical artery waveform still shows end-diastolic flow, reflecting an early adaptive process of the foetal heart in response to perinatal complications [4-6]. The Mod-MPI, also known as the Tei index, is a useful, yet somewhat rare, but important tool for assessing foetal cardiac function, especially in foetuses with Intrauterine Growth Restriction (IUGR).

The Mod-MPI measures both systolic and diastolic function of the heart and is calculated using Doppler ultrasound of the foetal heart [7-10]. With the deterioration of foetal cardiac function, foetal ventricular dysfunction occurs [11]. This is followed by reduced calcium reuptake in cardiac cells and an increase in the time required

for proper relaxation of the myocardium. IRT is the main Mod-MPI parameter that becomes abnormal in the very early stages of dysfunction. Reduced ET occurs, with ICT being the most stable Mod-MPI parameter [3].

Despite advances in the diagnosis and management of IUGR, there remains a small proportion of cases that face severe adverse perinatal outcomes, even in the presence of normal conventional Doppler studies. This highlights the need for new indices such as Mod-MPI to achieve better perinatal outcomes. The main aim of the study was to assess foetal cardiac function using Mod-MPI in IUGR foetuses in the third trimester and to compare Mod-MPI values with those of normal controls. Finally, the authors aimed to assess the role of the index in predicting perinatal outcomes in IUGR foetuses.

## MATERIALS AND METHODS

The prospective cohort study was conducted in the Department of Radiology at Government Medical College and Hospital, Coimbatore, Tamil Nadu, India, from May 2024 to December 2024. The study was carried out with prior informed consent from all participants, who

were provided with detailed explanations of the nature and course of the study and after obtaining approval from the Institutional Ethics Committee (ECR/892/Inst/TN/2016 No. 210/2024).

**Sample size calculation:** Sample size calculation was based on the study by Hamza HA et al., which showed a Mod-MPI value of 0.52 as the cut-off for the occurrence of adverse perinatal outcomes [12]. Assuming a desired power of 80% and a significance level (alpha) of 0.05, a total of 43 participants per group was determined as the required sample size.

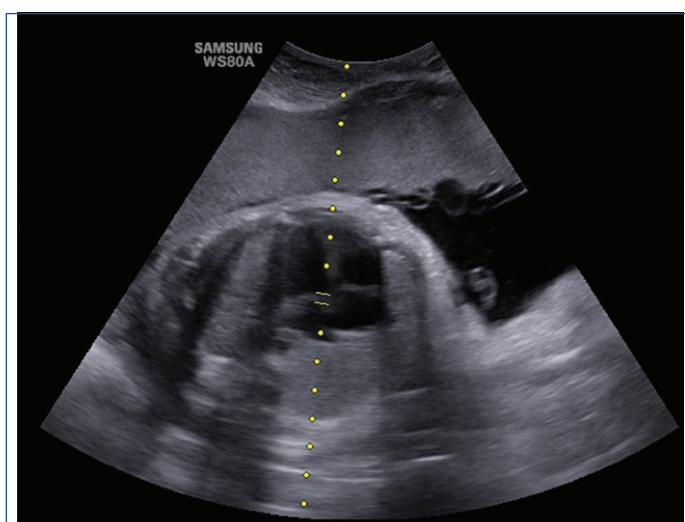
The IUGR cases were defined by an Abdominal Circumference/Estimated Foetal Weight (AC/EFW) less than the 3<sup>rd</sup> centile, or an AC/EFW less than the 10<sup>th</sup> centile with an umbilical artery Pulsatility Index (PI) >95<sup>th</sup> centile, or a Cerebroplacental Ratio (CPR) less than the 5<sup>th</sup> centile [13].

**Inclusion criteria:** Previous scan details were reviewed and cases with early onset (<32 weeks) IUGR were included in the study. A total of 43 singleton pregnancies in the third trimester with IUGR (cases) and 43 gestational age-matched normal singleton pregnancies in the third trimester (controls) were included in the study and followed until delivery. The control group was matched for gestational age, maternal age and parity. Controls were selected using purposive sampling to ensure balanced groups.

**Exclusion criteria:** Patients with twin pregnancies, congenital foetal anomalies, or a history of cardiac disease were excluded from the study.

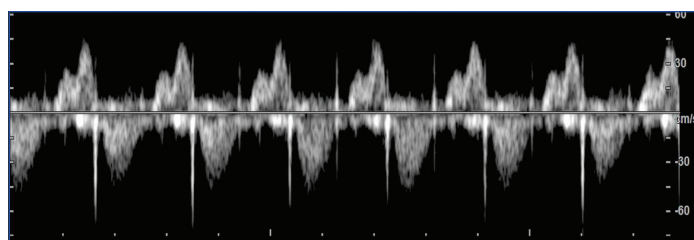
## Study Procedure

Ultrasound examinations were performed using a 2.5-5 MHz curvilinear transducer on a Samsung WS80A machine. All cases were studied by a single operator under the guidance of foetal medicine experts. A cross-sectional image of the foetal thorax at the level of the four-chamber view, with an apical projection of the heart, was obtained. By sweeping the ultrasound probe in the apical direction, the origin of the aorta could be visualised and the Doppler sample volume was placed in the internal leaflet of the mitral valve [Table/Fig-1]. Caliper placement was executed in the internal leaflet of the mitral valve, close to the aortic valve. In this position, due to its proximity to the aortic valve, the opening and closing clicks of the aortic valve could be recorded [Table/Fig-2]. The angle of insonation was maintained as close to 0 degrees as possible and was always <30 degrees [1]. The Doppler sweep speed was adjusted to 540 Hz, with the scale set to 45-55 cm/sec and the wall motion filter kept at 100 Hz.



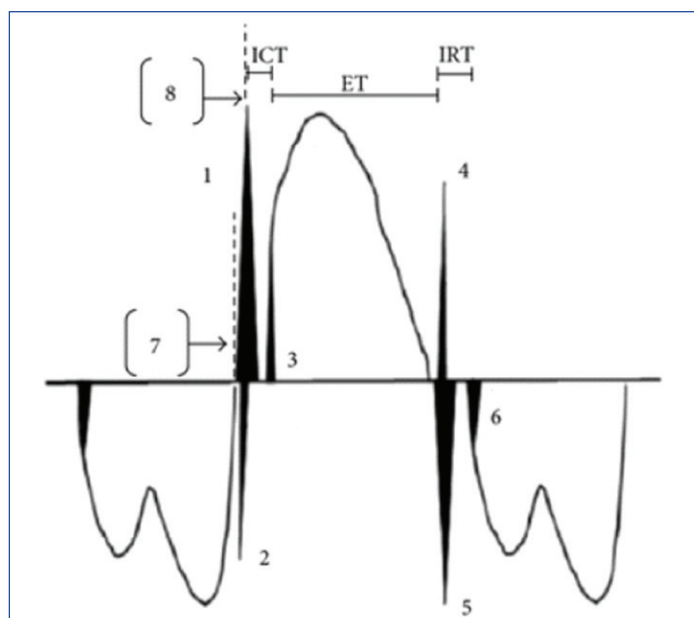
**[Table/Fig-1]:** Caliper placement in internal leaflet of mitral valve close to aortic valve.

The following three time periods were evaluated: ICT, IRT and ET. The Mod-MPI was calculated as (ICT+IRT)/ET [Table/Fig-3] [1,14]. The cases were followed until delivery and perinatal outcomes such as low birth weight, perinatal death, respiratory distress syndrome,

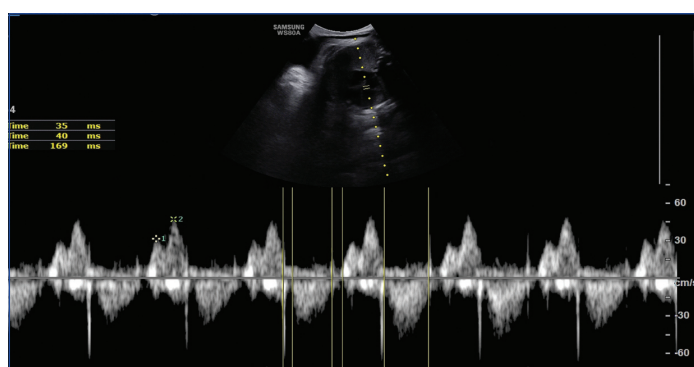


**[Table/Fig-2]:** Waveform obtained showing aortic valve clicks.

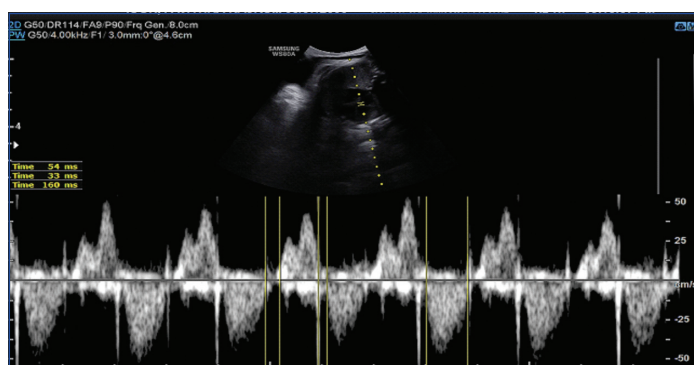
hypoxic-ischaemic encephalopathy, intraventricular haemorrhage and sepsis were recorded. Several representative cases are shown in [Table/Fig-4,5].



**[Table/Fig-3]:** Schematic diagram showing various time intervals measured for Mod-MPI calculation ICT: Isovolumetric Contraction Time, ET: Ejection time, IRT: Isovolumetric relaxation time: 1) Original MV closure click; 2) Reflected MV closure click; 3) Original AV opening click; 4) Reflected AV closure click; 5) Original AV closure click; 6) Original MV opening click; 7) Beginning of [1] (8) Peak of [1]. Adapted from Menki and Welsh [14].



**[Table/Fig-4]:** A normal case with various time intervals measured and Mod-MPI is 0.44.



**[Table/Fig-5]:** An IUGR case with various time intervals measured and Mod-MPI is 0.54.

## STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences version 24.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. The mean and SD of Mod-MPI were calculated. An Independent t-test was employed to examine variables with normal distribution. The Chi-squared test was used to assess the association between high Mod-MPI and adverse perinatal outcomes in both the IUGR cases and the control groups. The sensitivity and specificity at each cut-off value of the relevant predictor of adverse outcomes were determined and the area under the Receiver Operating Characteristic (ROC) curve was computed. A p-value of <0.001 was considered statistically significant.

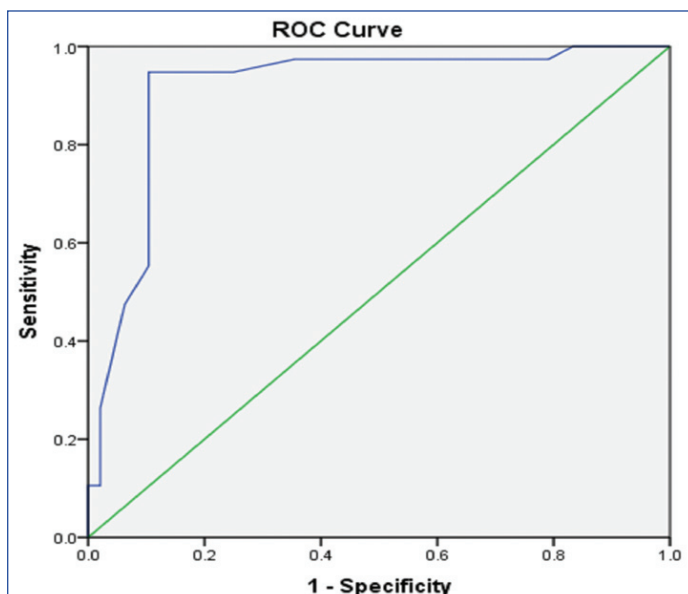
## RESULTS

The study enrolled women with a gestational age of 32 to 36 weeks in the third trimester and a maternal age ranging from 19 to 35 years. The mean gestational age and maternal age of the IUGR cases included in the study were  $34.2 \pm 1.5$  weeks and  $25.3 \pm 2.8$  years, respectively, while the corresponding values for the control group were  $34.5 \pm 0.6$  weeks and  $24.6 \pm 3$  years, respectively. Among the cases ( $n=43$ ), 21 (48.8%) were primiparous and 22 (51.2%) were multiparous. In the control group ( $n=43$ ), 22 (51.2%) were primiparous and 21 (48.8%) were multiparous. The distribution of parity between the case and control groups was nearly equal and not statistically significant ( $p$ -value=0.85). No statistically significant difference was found between the study and control groups concerning maternal age ( $p$ -value=0.27) and gestational age ( $p$ -value=0.42).

In IUGR cases, the mean Mod-MPI value was found to be 0.56 [Table/Fig-6]. In the present study, a Mod-MPI value of 0.4950 demonstrated the highest sensitivity and specificity according to the Receiver Operating Characteristic (ROC) curve [Table/Fig-7]. Therefore, this value was taken as a cut-off, where values at or above this threshold were considered indicative of a high Mod-MPI value associated with adverse perinatal outcomes. Among the 86 patients included in the study, 43 had Mod-MPI values below the specified cut-off, while the remaining 43 had Mod-MPI values above it. Of the 43 patients with Mod-MPI values below the cut-off, the majority-approximately 36 (83.7%)-were from the control group and

	Variables	Mean $\pm$ SD
Mod-MPI	Control	0.41 $\pm$ 0.05
	Case (IUGR)	0.56 $\pm$ 0.06
	p-value	0.001

[Table/Fig-6]: Mod-MPI values in Normal and IUGR group.  
Independent t-test



[Table/Fig-7]: Receiver Operator Characteristic (ROC) curve showed a significant relationship between Mod-MPI and adverse perinatal outcomes.

the remaining 7 (16.2%) were from the IUGR cases group. In the group of 43 patients with Mod-MPI values equal to or above the cut-off, the majority-about 40 (93%)-were from the IUGR group, with the other 3 (7%) belonging to the control group. Of these 43 patients with normal Mod-MPI values, only 3 (6.5%) experienced adverse perinatal outcomes. In contrast, among the 43 patients with high Mod-MPI values, 35 (87.5%) suffered adverse perinatal outcomes [Table/Fig-8].

Factors	Category	Total	Adverse perinatal outcome	Unadjusted odds ratio	95% CI*	p-value
			n (%)			
Mod-MPI	Normal values*	43	3 (6.5%)	7.47	3.28-17.04	0.001
	High values*	43	35 (87.5%)			

[Table/Fig-8]: Association of Mod-MPI with adverse perinatal outcome. Normal values\* indicates Mod-MPI values less than the cut-off of 0.4950 and High values\* indicated values more than or equal to the specified cut-off.  
Chi-square test

Nearly 85.3% of foetuses had adverse perinatal outcomes among the 37 foetuses that had normal conventional Doppler study results [Table/Fig-9]. Perinatal death was the most significant parameter, contributing to 18% in the IUGR cases group [Table/Fig-10]. The mean Mod-MPI value in cases of perinatal death was 0.53, with an SD of 0.04, which was higher than the specified cut-off. Among the controls, the only adverse perinatal outcomes recorded were two low-birth-weight babies, both of whom had a mean Mod-MPI value of 0.42.

Conventional doppler	Perinatal outcome		Total
	Normal	Adverse outcome	
Normal	6 (14.7%)	31 (85.3%)	37
Abnormal	0	6 (100%)	6
Total	6 (12.5%)	37 (87.5%)	43

[Table/Fig-9]: Perinatal outcome in high MOD-MPI foetuses depending upon their conventional doppler.

Perinatal outcome	IUGR cases	Controls	p-values*
Perinatal death	8 (18%)	0	<0.001
Low birth weight	32 (74%)	2 (4%)	<0.001
NICU admission	20 (46%)	0	<0.001
Respiratory distress syndrome	7 (16%)	0	<0.001
Hypoxic ischaemic encephalopathy	13 (30%)	0	<0.001
Intraventricular haemorrhage	4 (9%)	0	<0.001
Sepsis	4 (9%)	0	<0.001

[Table/Fig-10]: Perinatal outcome in cases and controls.  
\*Chi-square test; NICU: Neonatal intensive care unit

The values of Mod-MPI are plotted in the ROC curve under the coordinates shown in [Table/Fig-7]. The area under the curve was 0.98. In terms of actual Mod-MPI values, a cut-off of 0.4950 was associated with a sensitivity of 92% and a specificity of 83%. Consequently, this value was taken as a cut-off in the present study for predicting adverse perinatal outcomes. The positive and negative predictive values were found to be 81% and 93%, respectively, with an accuracy of 87%.

## DISCUSSION

Intrauterine foetal growth restriction is a very common condition that has significantly high perinatal morbidity and mortality. The present study showed that the mean Mod-MPI values were higher in the IUGR group ( $0.56 \pm 0.06$ ) than in the control group ( $0.41 \pm 0.05$ ). The difference in these values was significant. This correlates with the study conducted by Nassr AA et al., which states that the mean left MPI was significantly higher in IUGR foetuses with abnormal UA Doppler (mean  $0.58 \pm 0.093$ ) compared with healthy foetuses (mean



0.45±0.070) (p-value <0.001) [15]. These values also align with the study conducted by Nair A and Radhakrishnan S, which reported that the normal values of Mod-MPI in the Indian population were 0.42±0.03 [16].

Out of the various perinatal outcome parameters studied, the occurrence of perinatal deaths accounted for 18%. A statistically significant association was noted between Mod-MPI and adverse perinatal outcomes (p-value <0.001). This correlates with a study conducted by Zhang L et al., which concluded that Mod-MPI values are higher in fetuses with growth restriction and can be used to predict adverse perinatal outcomes [17].

In the present study, fetuses with high Mod-MPI had a 7.47 times higher risk of experiencing adverse perinatal outcomes. This is consistent with a study conducted by Bhorat IE et al., [18], which concluded that there is an association between the severity of Mod-MPI elevation and the rates of adverse perinatal outcomes.

Nearly 85.3% of fetuses with high Mod-MPI and normal conventional Doppler showed adverse perinatal outcomes. In the IUGR group, both normal and abnormal Doppler displayed higher MPI when compared to the control group. This suggests that the rise in Mod-MPI values preceded changes in conventional Doppler studies in the present study. This finding is in accordance with a study conducted by Zhang L et al., [17], which states that impairment of myocardial function might occur earlier than haemodynamic changes, as there was no significant difference in Mod-MPI between normal and abnormal Doppler cases. This is also supported by the study done by Czapska AH and Kosinska-Kaczynska K, which indicates that Mod-MPI values are altered before arterial doppler parameters, making it feasible to identify at-risk fetuses at an early stage of cardiac dysfunction [19]. Only 5.9% of the cases with high Mod-MPI values had a normal perinatal outcome. Another study by Kaarthiga RG et al., predicted that high MPI values were found in all IUGR fetuses, with a mean of 0.65±0.11 and significantly predicted perinatal outcomes such as NICU admission [20].

Apart from the early detection of adverse perinatal outcomes, Mod-MPI also assesses early cardiac dysfunction, identifies compensatory mechanisms and evaluates the effectiveness of interventions, such as the administration of corticosteroids. Among previous studies evaluating Mod-MPI values in gestational diabetes mellitus in relation to perinatal outcomes, one concluded that the diabetic group with adverse outcomes had significantly elevated MPI values compared to the diabetic group with normal outcomes, underscoring the significance of foetal Mod-MPI in gestational diabetes mellitus [21]. Additionally, prior studies indicate that fetuses in pregnancies complicated by placenta previa exhibit impaired cardiac function, as evidenced by elevated Mod-MPI values [22].

In some earlier studies, corticosteroid administration in IUGR fetuses has been linked to a significant decrease in right ventricular Mod-MPI, suggesting improved right ventricular function [23]. One study observed a reduction from 0.56 to 0.47 (p-value=0.007) following corticosteroid exposure. Conversely, the same study noted no significant change in left ventricular Mod-MPI after corticosteroid administration in IUGR cases, with values remaining relatively stable (from 0.49 to 0.48) [23]. It is crucial to recognise that the administration of corticosteroids can influence foetal cardiac output, which may complicate the interpretation of Mod-MPI in cases of growth restriction or other complex pregnancies. Therefore, it is essential to monitor any changes in cardiac function following corticosteroid treatment to ensure accurate evaluation [24].

### Limitation(s)

A small sample size, along with the need for further multicentric trials and larger sample groups, is necessary to confirm the results. Additionally, cardiac time intervals are measured through the subjective placement of calipers on doppler ultrasound waveforms, so the possibility of intra- and interobserver errors cannot be excluded

from the study. Future efforts should consider the automation of the measurement process.

## CONCLUSION(S)

The Mod-MPI is a simple and sensitive parameter for early foetal cardiac adaptation. Higher MPI values are significantly associated with adverse perinatal outcomes, even in the presence of normal conventional doppler findings. The integration of Mod-MPI into routine foetal surveillance would aid in classifying patients into high- and low-risk groups, thereby improving perinatal outcomes.

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