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RESEARCH

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Role of prenatal fetal echocardiography in the assessment of intrauterine growth restriction

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Abstract

Background: Intrauterine growth restriction (IUGR) is a common diagnosis in obstetrics and carries an increased risk of perinatal mortality and morbidity. Identification of IUGR is crucial because proper evaluation and management can result in a favourable outcome. Cardiovascular dysfunction and remodelling is a central feature of IUGR. The aim of the study was to use the left modified myocardial performance index (MPI), assess cardiac function in foetuses with intrauterine growth restriction (IUGR) compared to healthy foetuses, and to connect the relationship between changes in MPI and perinatal outcome. A prospective study was conducted with 60 singleton foetuses between 24 and 40 weeks of gestation without foetal chromosomal abnormalities or major malformations, divided into two groups: 30 women with intrauterine growth restriction (30 women) and another 30 women with normal pregnancies (foetal growth pattern appropriate for gestational age and normal heart findings with normal sinus rhythm) who were matched for gestational age and served as the controls. Trans-abdominal ultrasound examination was done with 3.5–7-MHz curvilinear Probe (GE Medical US equipment). The umbilical arteries, middle cerebral artery, and ductus venosus all had blood flow velocity waveforms recorded. The pulsatility index (PI), cerebroplacental ratio (CPR), and Doppler velocimetry (DV) of the umbilical artery were all measured. All foetuses had their myocardial performance index assessed. Normal and abnormal umbilical artery(UA) Doppler, as well as normal and abnormal MCA Doppler, were used to examine the intrauterine growth restriction group. Foetal growth restrictions (FGR) foetuses' Mod-MPI values were compared to gestation-matched controls. The outcomes of the perinatal period were documented.

Results: Intrauterine growth restriction foetuses with defective umbilical arteries Doppler had a substantially higher mean left myocardial performance index (mean 0.58 SD 0.093) than healthy foetuses (mean 0.45SD 0.070) (P 0.001). When compared to the control group, IUGR foetuses with abnormal left myocardial performance index had a significantly worse perinatal outcome and higher morbidity. When compared to intrauterine growth restriction foetuses with normal MPI, intrauterine growth restriction foetuses with defective left MPI had a significantly worse perinatal outcome (whether the UA Doppler was normal or abnormal). Based on the perinatal result, the foetal myocardial performance index was linked to the severity of foetal impairment in intrauterine growth restriction foetuses.

Conclusion: MPI has the potential to be a useful technique for evaluating IUGR pregnancies and predicting neonatal outcome. Within the IUGR foetuses, MPI foetal echocardiographic characteristics can define a high-risk group.

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Keywords: Myocardial performance index, Foetal echocardiography, MPI, Perinatal outcome, Umbilical artery Doppler, Intrauterine growth-restricted foetus

Background

In clinical practices, foetal growth restriction (FGR) has proven to be a difficult problem. It has a strong link to a poor perinatal outcome. Prematurity, respiratory distress syndrome, and necrotizing enterocolitis are all FGR complications that have increased neonatal mortality and morbidity [1].

Monitoring and detecting FGR during pregnancy is a vital procedure, as it informs the timing and mode of delivery, thereby improving the case's result. The umbilical artery (UA), middle cerebral artery (MCA), and ductus venous Doppler measures have all been used to assess the intrauterine safety of foetuses. The alterations in Doppler flow in these veins indicate that the cardiovascular status of foetuses is deteriorating. The Doppler flow spectra of certain FGR foetuses, on the other hand, stay normal until a poor neonatal outcome occurs. As a result, finding an effective metric to supplement FGR monitoring is critical [2].

Tei index (myocardial performance index) is a Doppler echocardiography tool for evaluating cardiac ventricular systolic and diastolic functioning [3].

Relevant studies revealed that aberrant MPI occurs early in the course of foetal deterioration, before abnormal Doppler findings in specific arteries and a decrease in amniotic fluid volume (oligohydramnios) in IUGR foetuses [4].

Monitoring cardiac function in IUGR foetuses has been advocated as a supplement to current approaches for predicting severe perinatal outcomes. Furthermore, earlier research has shown that a fraction of intrauterine growth restriction cases had a higher MPI value than foetuses of appropriate gestational age (AGA) [5].

The objective of this study was to use the left modified myocardial performance index (MPI) to assess heart function in foetuses with intrauterine growth restriction (IUGR) and to connect changes in MPI with perinatal outcome.

Methods

The present prospective study was carried out on patients divided into two groups: 30 women with IUGR and another 30 women with normal pregnancies with foetal growth pattern appropriate for gestational age and normal heart findings with normal sinus rhythm. The control group was matched for gestational age to our patients.

The cases for the study were referred to the radiology department at our institution from the gynaecology and obstetrics department. All of the patients gave their informed consent, and the study was authorised by the local ethics committee.

The gestational age was determined using the latest menstrual period and validated using a first-trimester ultrasound.

Inclusion criteria

Included: pregnant women with singleton foetuses between 24 and 40 weeks of gestation, and foetuses have been diagnosed with IUGR. The IUGR diagnosis had been based on abdominal circumference [AC] below the 10th percentile for gestational age and/ or the estimated foetal weight [EFW] below the 10th percentile for gestational age; and/or abnormal foetal Doppler indices Umbilical artery pulsatility index [PI] more than 95th percentile for gestational age or resistibility index [RI] more than 95th percentile for gestational age.

Exclusion criteria

Included any pregnancy that was complicated by known aneuploidy, foetal cardiac anomaly, Major/multiple congenital anomaly suggesting a syndromal cause for FGR or preterm premature rupture of membranes.

Demographic characteristics, including age, gravidity, parity, and maternal body mass index (BMI), were recorded, in addition to obstetric and medical histories, gestational age.

Ultrasound examinations were performed using a Loqic (GE Medical Systems), equipped with a 3.5–7-MHz curvilinear transducer. Some cases were done by more than one author (having about 7 years of experience) to avoid subjective bias.

The umbilical artery (UA) pulsatility index (PI) was evaluated in a free loop of cord away from foetal insertion or placental insertion sites.

The pulsatility index (PI) of the middle cerebral artery (MCA) was measured near the MCA origin in the internal carotid artery in the proximal portion of the artery. Willis' circle was identified using colour flow mapping. The insonation angle was set as close to 0° as practicable. By dividing the MCA pulsatility index by the UA pulsatility index, the cerebroplacental ratio (MCA/UAPI) was computed.

A mid-sagittal image of the foetal trunk was used to calculate the PI of the ductus venosus (DV) or through the upper abdomen in a transverse plane before to its entry into the inferior vena cava, with the Doppler gate positioned at the ductus venosus isthmic part. A conventional sampling location with high velocity at its narrow entry was identified using colour flow mapping.

The cardiothoracic ratio was calculated by dividing the heart area by the thoracic area in cardiac morphometry.

For reliable measurement of the left myocardial performance index, some machine settings were modified, including fastest Doppler sweep velocity (13.8–15 cm/s), angle of insonation 0–15; Doppler gain low; wall motion filter 300 Hz.

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 to evaluate the left myocardial performance index. The Doppler sample volume was positioned on the ascending aorta's lateral wall, including the aortic and mitral valve leaflets. At the beginning and end of the E/A (mitral valve) and AF (aortic valve) waveforms, the Doppler trace exhibited a distinct echo matching to the opening and closing of the two valves. The Doppler trace clicks were used as landmarks to calculate the following time periods: isovolumetric contraction time from the closure of the mitral valve to the opening of the aortic valve, ejection time from the opening to the closure of the aortic valve, and isovolumetric relaxation time from the closure of the aortic valve to the opening of the mitral valve. Finally, the myocardial performance index was derived as (isovolumetric contraction time minus isovolumetric relaxation time) / ejection time. The spectral Doppler of ventricular inflow as E and A waveforms, as well as outflow, could then be shown at the same time.

All estimations were done in the absence of foetal corporal and respiratory movements. Foetal heart rate was calculated on spectral Doppler imaging.

Gestational age, delivery mode, birthweight, birthweight centile, Apgar score, and perinatal mortality and morbidity were all reported at the time of delivery. Any of the following was considered an adverse perinatal outcome: perinatal death, neonatal resuscitation, hypoxic ischaemic encephalopathy, neonatal pH 7.5, intraventricular haemorrhage, and bronchopulmonary dysplasia are all terms used to describe perinatal death, neonatal resuscitation, hypoxic ischaemic encephalopathy, neonatal pH 7.5, intraventricular haemorrhage, and bronchopulmonary dysplasia.

Statistical analysis

Continuous variables were summarized as mean and standard deviation, while nominal/categorical variables were summarized as proportion. Parametric test will be used for continuous variable, whereas Chi-square test and Fisher's exact test will be used for nominal/categorical variability. P value < 0.05 will be taken as significant value.

Results

Our study included 30 pregnant patients with IUGR and another 30 gestation-matched controls pregnant females. The demographic maternal characteristics of both groups are reported in Table 1. Mean age for the pregnant women was 28.9 ± 3.3 years in the study group and 28.7 ± 2.9 years in the control group. No significant difference in maternal age (P value 0.804) was observed between the groups. The mean gestational age [GA] at enrolment was 30.80 ± 3.42 weeks for the study group compared to 30.5 ± 3.17 weeks for the control group (P value 0.726).

The mean abdominal circumference (AC) percentile measurements of the foetuses in the study group (Table 2) were significantly lower than those of foetuses in the control group: 2.51 ± 0.73 and 50.62 ± 23.12,

Table 1 Maternal characteristics among the control and IUGR groups

Maternal characteristics	Control group (n = 30)	IUGR group (n = 30)	*Test value*	*p* value
Age (years)				
Mean ± SD	28.7 ± 2.9	28.9 ± 3.3	$t = 0.249$	0.804
Range	24.2–34.5	24.3–34.3		
BMI(Kg/m^2)				
Mean ± SD	29.2 ± 3.3	30.3 ± 3.4	$t = 1.272$	0.209
Parity				
Primipara	12 (40%)	14 (46.7%)	$x^2 = 0.068$	0.795
Multipara	18 (60%)	16 (53.3%)		
GA at Exam (Wks.)				
Mean ± SD	30.5 ± 3.17	30.8 ± 3.42	$t = 0.352$	0.726
Range	24.2–35.5	24.4–35.6		

t, Independent Sample t test; χ^2, Chi-square test

p value > 0.05 NS

Table 2 Percentiles distribution of the abdominal circumference and estimated foetal weight among control and IUGR groups

Variable	Control group (n = 30)	IUGR group (n = 30)	*t test*	*p* value
AC percentiles				
Mean ± SD	50.62 ± 23.12	2.51 ± 0.73	11.392	< 0.001**
Range	32.56–69.4	2.1–2.93		
EFW percentiles				
Mean ± SD	45.73 ± 22.3	3.29 ± 0.79	10.417	< 0.001**
Range	28.1–58.4	3.1–3.34		

t, Independent Sample t test

***P* value < 0.001 HS

Table 3 Findings of Doppler US of the umbilical, middle cerebral arteries and DV with corresponding MPI in IUGR foetuses

Doppler parameter	No	%
UAPI		
Normal	5	16.70
> 95th	25	83.30
UA Diastolic flow		
Ante grade	26	86.70
Reversed	4	13.30
MCA PI		
Normal	24	80.00
< 5th	6	20.00
CPR		
> 1	22	73.30
< 1	8	26.70
DV (a wave)		
Ante grade	27	90.00
Reversed	3	10.00
MPI		
Normal	6	20.00
Increased	24	80.00

UAPI umbilical artery pulsatility index, *MCAPI* middle cerebral artery pulsatility index, *CPR* cerebroplacental ratio

respectively ($p < 0.001$). Moreover, the EFW percentile measurements were 3.29 ± 0.79 in the study group and 45.73 ± 22.3 in the control group, and the difference was significant ($p < 0.001$).

Blood flow through the umbilical and middle cerebral arteries was assessed by Doppler US in both groups with measurement of pulsatility indexes. Among 30 foetuses with IUGR, 25 (83.3%) have abnormal PI of the umbilical arteries, four of them showed reversed end diastolic blood flow of the umbilical arteries. In six foetuses, decreased pulsatility index of the MCA was seen. On the other hand, CPR was found to be decreased in eight foetuses (Table 3). Two foetuses had reversed DV a wave. Among 30 IUGR foetuses, the left MPI was increased in 24 foetuses having values ranged between 0.52 and 0.70 [mean ± SD 0.61 ± 0.08).

Foetal MPI and its time periods components among control and IUGR foetuses were included (Table 4). The IVRT (Fig. 1) was longer (mean 54.3 ± 3.3) and ejection time was shorter (mean151 ± 4.47 SD) in IUGR foetuses (Fig. 2) compared with control group. On the other hand, IVCT did not show significant variation between control and IUGR groups (*P* value 0.886). The mean myocardial performance index was 0.58 ± 0.02

Table 4 Time period's components of the MPI among control and study groups

Measured time	Control Group (n = 30)	IUGR Group (n = 30)	*t test*	*p* value
IVRT	41.13 ± 2.91	54.3 ± 3.3	16.395	< 0.001**
IVCT	34.02 ± 2.84	34.12 ± 2.51	0.145	0.886
ET	170.61 ± 6.45	151 ± 4.47	13.687	< 0.001**
MPI	0.44 ± 0.01	0.58 ± 0.02	34.293	< 0.001**

t = Independent Sample t test

P value > 0.05 NS

**P* value < 0.05 S

***P* value < 0.001 HS

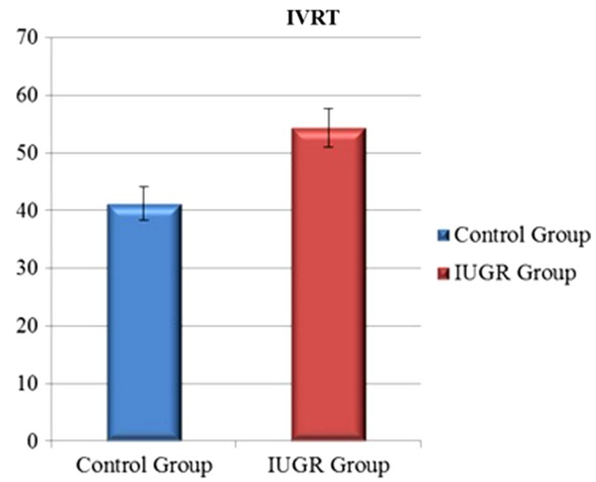

Fig. 1 Comparison between control and IUGR groups according to IVRT

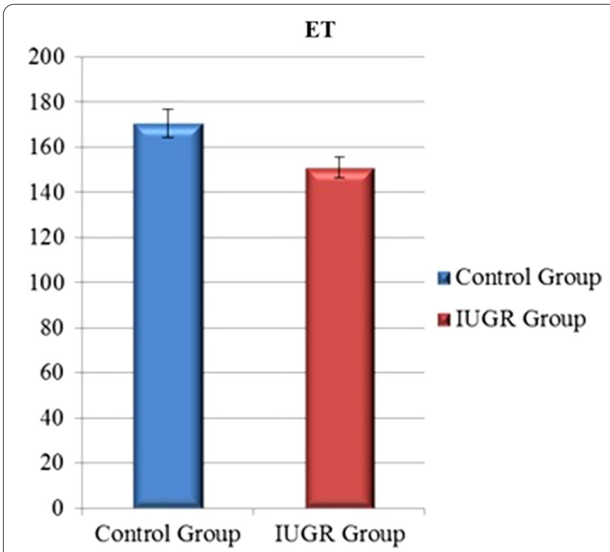

Fig. 2 Comparison between control and IUGR groups according to ET

in IUGR group (Fig. 3), while in control group, it was 0.44 ± 0.01. That result was statistically significant (*P* value < 0.001).

Delivery was started in accordance with standard obstetric practice guidelines at our institution. The majority of the IUGR foetuses (83.3%) were delivered by CS due to repeated CS: 16 cases, breech presentation: 3 cases, foetal distress: 3 cases and placenta previa: 3 cases. On the other hand, ten foetuses of the control were delivered by CS: eight cases had previous CS and two cases had breech presentation.

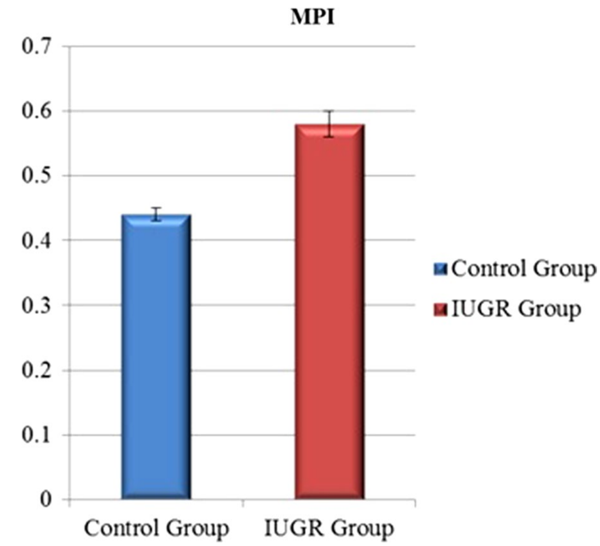

Fig. 3 Comparison between control and IUGR groups according to MPI

The mean gestational age at delivery of the control was at near term (38 ± 1.0 weeks) and revealed a statistically significant difference from that of the IUGR group (34 ± 0.9) ($P < 0.05$).

Pregnancy outcomes are shown in (Table 5). Among six foetuses with IUGR and normal MPI (Fig. 4), only two foetuses had adverse perinatal outcome, showing meconium stained AF (Fig. 5), one of them had apgar score at 5 min < 7 showing need for neonatal resuscitation. The mean 5-min Apgar score of the control group was significantly higher than the IUGR foetuses with increased MPI.

When compared to normal pregnancies, IUGR foetuses with defective MPI had a significantly lower perinatal fate. When compared to six IUGR foetuses with normal left MPI, 24 IUGR foetuses with elevated left MPI had a worse perinatal outcome (Fig. 6). (Table 6).

Discussion

The left modified myocardial performance index (MPI) was used to assess cardiac function in foetuses with intrauterine growth restriction (IUGR) compared to healthy foetuses and to connect the relationship between changes in MPI and perinatal outcome.

The foetal myocardial performance index (MPI) has been developed for this purpose [6]. It is a Doppler-derived global measure of foetal ventricular function that is rather simple to obtain.

The foetal adaptation to undernutrition and hypoxia in the presence of pressure/volume overload due to enhanced placental resistance was postulated in FGR [7].

Table 5 Route of delivery and perinatal outcome in the control and IUGR foetuses (with normal and abnormal MPI)

Studied group	Route of delivery		Apgar score at 5Min < 7	Meconium stained AF	Need for NR	NICU Admission
	Vag	CS				
Control (n = 30)	20	10	1	2	1	0
IUGR with normal MPI (n = 6)	2	4	1	2	2	0
IUGR with increased MPI (n = 24)	3	21	7	5	16	10
P value	P^a	< 0.001**	0.017*	0.221	< 0.001**	< 0.001**
	P^b	0.181	0.309	0.121	0.066	1.000

FE Fisher's Exact, *S.AF* amniotic fluid, *NR* neonatal resuscitation, *NICU* neonatal intensive care unit

**p* value < 0.05

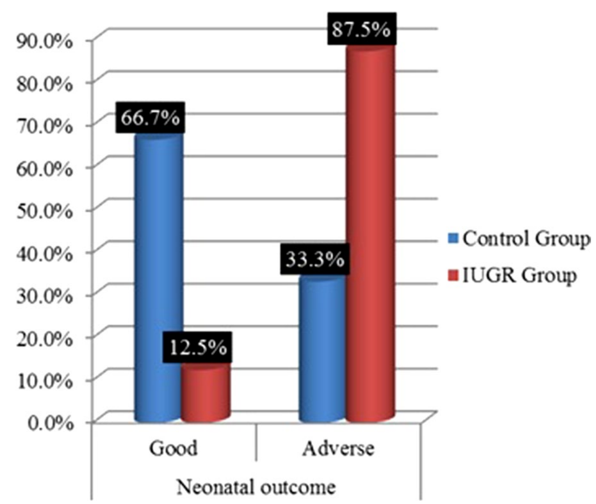

Fig. 4 Perinatal outcome in IUGR group with normal and increased MPI

Results of the present study revealed that in IUGR babies with aberrant UA Doppler, the mean left MPI was considerably greater than in healthy normal foetuses during our research. Furthermore, when compared to the control group, IUGR foetuses with aberrant left ventricular MPI had a significantly inferior perinatal outcome and greater morbidity. When compared to IUGR pregnancies with normal foetal left MPI, IUGR foetuses with aberrant left MPI had a considerably lower perinatal prognosis (whether the UA Doppler was normal or abnormal). We also noticed that the severity of foetal compromise in IUGR was determined by the degree of deterioration of the left foetal MPI, as judged by the perinatal outcome in our three foetuses with frank abnormal left ventricular MPI, and these foetuses had significantly worse perinatal outcomes than the control group.

This result is in agreement with the findings of Bhorat et al. [8], who found that MPI is a potentially effective technique in evaluating foetuses with suspected IUGR, which is vital in distinguishing critical and non-critical IUGR cases and predicting neonatal prognosis. These findings are consistent with those of Ahmed et al. [9], who found a link between foetal cardiac function degradation and the progression of foetal compromise in IUGR, and Alici et al. [10], who found MPI to be beneficial in predicting poor perinatal outcome in IUGR.

During our study,we compared the time periods components of the myocardial performance index among the control and the IUGR groups, we demonstrated that the IVRT was longer (mean 54.3 ± 3.3) and ejection time was shorter (mean151 ± 4.47 SD) in IUGR foetuses compared with control group. On the other hand, IVCT did not show significant variation between control and IUGR groups (*P* value 0.886).

This is in line with a study by Zhang et al. [11], who found that ventricular dysfunction is linked to higher MPI values, which they attribute to IVRT prolongation. With a change in cardiac function, reduced calcium reuptake of cardiac cells occurs, which can lead to a prolonging of complete cardiomyocyte relaxation, resulting in an increase in the time necessary to relax the myocardium properly. As a result, the IVRT is the primary MPI parameter that becomes aberrant early in the course of dysfunction.

Prolonged IVRT may be an early indication of cardiac dysfunction common to numerous illnesses, according to Bravo-valenzuela et al. [12], with the common link being an increase in preload with subsequent diastolic dysfunction. With the IVCT being the most stable MPI parameter, a greater IVRT is usually accompanied by a lower ET.

During our study, in six foetuses with IUGR, decreased pulsatility index of the MCA was seen. On the other hand, CPR was found to be decreased in eight foetuses, all of them showed adverse perinatal outcome.

This is congruent with Figueras et al. [13], who reported that the CPR, which combines the pulsatility index of the MCA and UA, is more sensitive to hypoxia (defined as a reduced partial pressure of oxygen [pO2]

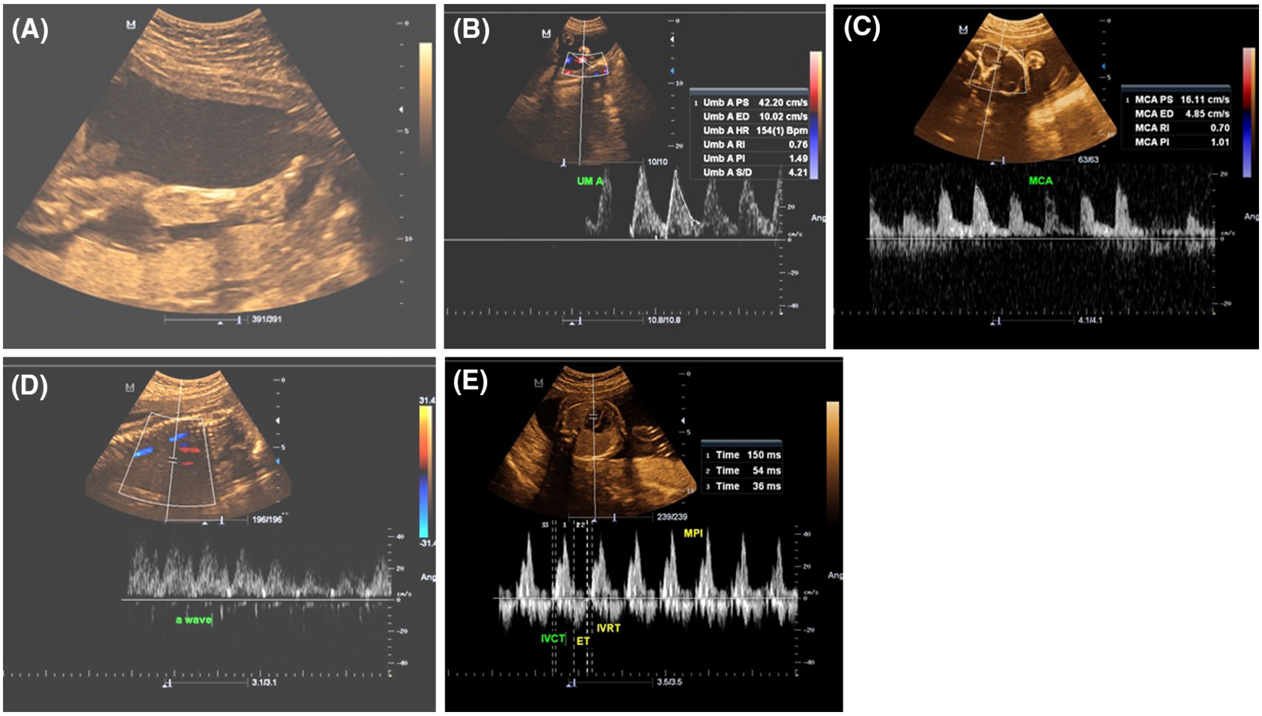

Fig. 5 A 28-year-old primigravida patient, was examined at 34 weeks gestation, had an US foetal age of 31 weeks and foetal weight of 1860 gm. **A** US showing marked turbidity of amniotic fluid (Meconium). **B** Doppler US of umbilical artery showing increased pulsatility index. **C** Colour Doppler assessment of middle cerebral artery (MCA) in a growth-restricted foetus showing high diastolic velocities and decreased pulsatility index. **D** US Doppler spectrum of foetal DV showing reversed a wave. **E** Doppler trace of isovolumetric contraction time, ejection time, isovolumetric relaxation time for assessment of left ventricular MPI

in the arterial system) than its individual components and correlates better with adverse outcomes.

During our study, we chose to assess the left MPI, where a single waveform could be used to measure the time components of the myocardial performance in the left ventricle.

Meriki et al.[3] revealed that, while the embryonic heart is right ventricle dominant, examination of the right ventricle might reveal certain early indications of cardiac dysfunction. The right MPI, on the other hand, necessitates different waveforms for tricuspid and pulmonary flows and could be altered by foetal heart rate fluctuations.

MPI evaluation of the right ventricle requires a two-plane image and two different waveforms for the pulmonary and tricuspid valves, according to Porche et al. [14], and can be influenced by variations in foetal heart rate, making right heart assessment problematic. The flows of the aorta and mitral valves, on the other hand, can be conveniently analysed in the same Doppler image because of the left heart's distinctive structure. Because of the advantages of the left heart and the intricacy of the right heart, it was decided to get left ventricular MPI rather than right ventricular MPI.

Limitations of the study

We encountered many difficulties during the ultrasound examinations including poor image quality due to maternal habitus and obesity and previous abdominal scar. Unsuitable foetal posture can add to the difficulty during US examination. However, this problem could potentially be overcome by various techniques. Newer imaging modalities such as tissue harmonic imaging allow detection of higher frequency ultrasound waves and produce a higher resolution image in obese women. Other limitation was the limited no. of patients in the study due to referral of most of the cases to Gynecological/Obstetric department.

Conclusions

Early stages of cardiac adaptation associated with increasing placental vascular resistance in growth-restricted foetuses are represented by changes in MPI and its time period components. It can be used in foetal assessment in cases of intrauterine foetal growth restriction because of its high sensitivity, relative ease of use, and information offered by the MPI. Regardless of the UAPI's Doppler findings, foetuses with an EFW 10th centile may be evaluated for MPI and CPR evaluation.

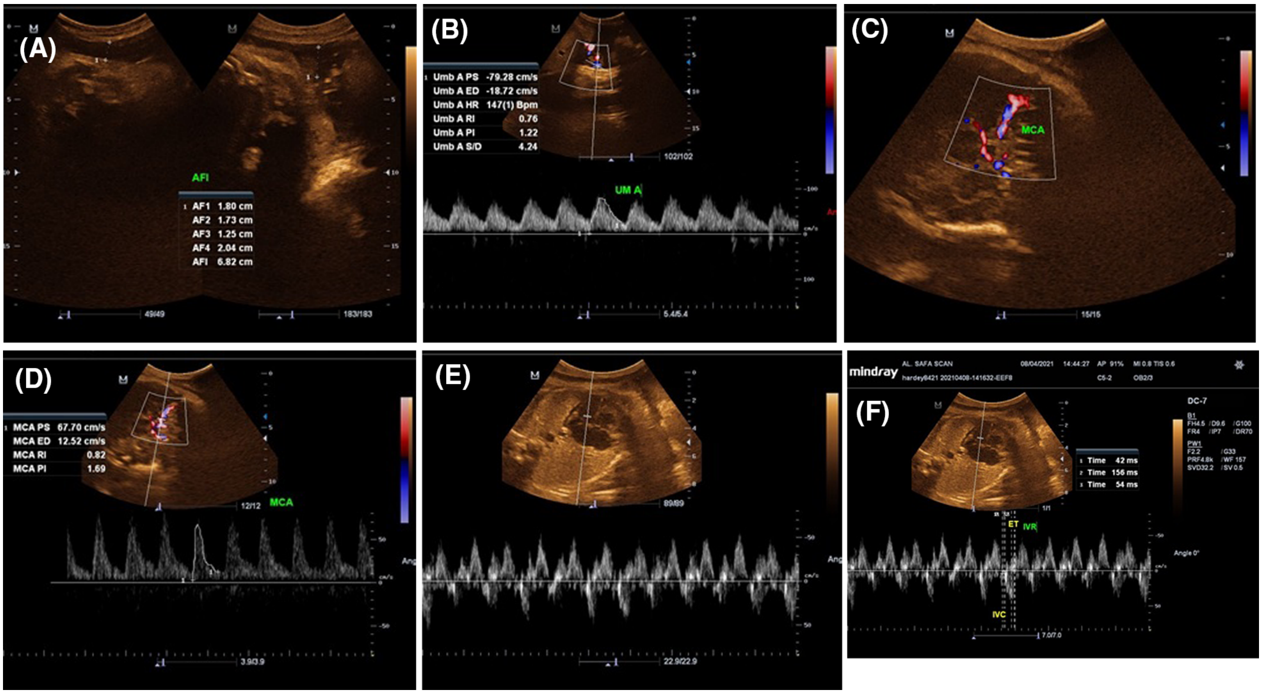

Fig. 6 A 33-year-old patient was examined at 32 weeks gestation, had an US foetal age of 28 weeks and foetal weight of 1050 gm. **A** Ultrasound showing oligohydramnios with decreased amniotic fluid index. **B** Doppler US of umbilical artery showing increased pulsatility index with preserved antegrade diastolic waveform pattern. **C** and **D** Colour Doppler assessment of middle cerebral artery (MCA) in a growth-restricted foetus. A, at level of circle of Willis.B, flow velocity waveform with normal pulsatility index of MCA. **E** Apical 4-chamber view of the foetal heart showing location of the sample volume on the internal wall of the ascending aorta, close to the internal leaflet of the mitral valve and below the aortic valve for measurement of the left Mod-MPI. Myocardial performance index (MPI) measured in the left ventricle. The Doppler waveform displays the clicks of aperture and closure of the mitral and aortic valves. **F** showing reference points for time periods estimations for measurement of IVCT, ET and IVRT based on echoes from the opening and closure of the mitral and aortic valves with a calculated MPI = 0.61

Table 6 Perinatal outcome in IUGR group with normal and increased MPI

Neonatal outcome	MPI				*p* value[a]
	Normal (n = 6)		Increased (n = 24)		
	No	%	No	%	
Good	4	66.7	3	12.5	0.016*
Adverse	2	33.3	21	87.5	

[a] FE: Fisher's Exact

**p* value < 0.05

Abbreviations
MPA: Myocardial performance index; UAPI: Umbilical artry pulstility index; CPR: Cerebroplacental ratio; US: Ultrasound; UA: Umbilical artery; DV: Ductus venosus; IUGR: Intrauterine growth restriction.

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Author contributions
NSAAA (corresponding author) collected the patients' data, evaluated the patients' clinical symptoms, performing foetal echocardiography studies for collected patients and also contributed to manuscript writing and editing. FSEM revised the data and helped in statistical analysis. NAT interpreted the data collected and analysed it. HGEMAH performed foetal echocardiography studies sharing in reviewing literature and verified manuscript editing. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study is approved by Ain Shams University ethical and scientific committee. A written informed consent is obtained from all patients before the procedure.

Consent for publication
Consent for publication was obtained for every individual persons' data included in the study.

Competing interests
The authors declare that they have no competing interests.

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