

Impact Of Fetal Modified Myocardial Performance Index in Evaluating Cardiac Function In Cases Of Diabetic Pregnancies And Preeclampsia

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Abstract

The myocardial performance index (MPI) was first proposed by Tei et al. as a means of assessing heart function in patients suffering from dilated cardiomyopathy. The MPI derived from Doppler has shown potential as a non-invasive measure of global myocardial function. The maximum pressure index (MPI) is obtained by subtracting the ejection time (ET) from the total isovolumetric contraction and relaxation times (ICT and IRT, respectively). Tsutsumi et al. were the first to note that the MPI might be used to assess the fetal heart's overall function. The MPI has been proposed by other researchers as a potential useful tool for predicting fetal cardiac adaptation alterations in complicated pregnancies involving growth-restricted fetuses, fetuses of diabetic mothers, fetuses with heart failure (including hydropic fetuses), and fetuses with Rh sensitization. Conversely, reference MPI values for left fetus cardiac assessment span a wide range in published literature. The big difference between the usual reference values is believed to be caused by the lack of distinguishing characteristics in the Doppler waveforms that were used to calculate the time-periods. In an attempt to circumvent this problem, other authors have proposed different alternatives. The Mod-MPI, developed by Hernandez-Andrade et al., is an adaptation of the myocardial performance index. Improved agreement and lower variation compared to the original MPI were seen with this adjustment, which is based on Doppler echoes of the aortic and mitral valves. Due to its new addition to the literature, Mod-MPI has not been used to evaluate fetal cardiac function in relation to pregnancy-related complications.

Key words: Fetal cardiac performance index impact.

1. Introduction

Preeclampsia, which affects around 2% of pregnancies, is a major cause of maternal and newborn illness and mortality. Problems with placental implantation and the success (or failure) of trophoblastic invasion have been proposed as potential causes of preeclampsia, however the exact mechanism is still unclear. It is thought that insufficient trophoblastic invasion of the mother's spiral arteries is the source of circulation resistance in the uteroplacental system. One potential effect of the foetal cardiovascular system's higher vascular placental resistance is an increase in the fetal cardiac afterload.

One medical condition that supposedly boosts the MPI, according to new study, is an increase in cardiac afterload caused by increased placental vascular resistance. We hypothesised that, since preload and afterload have such a profound effect on cardiac contractility, preeclamptic women could have fetal cardiac function that is impaired. Although there is a lack of data on foetal cardiac function in preeclampsia, a recent study on infants delivered to mothers with moderate preeclampsia revealed cardiac dysfunction and mild myocardial damage.

Using MPI, a simple and effective approach, it is easy to evaluate the fetal ventricular function. It is well-documented that fetal cardiac output redistributes to the left ventricle in complicated pregnancies, and that fetal circulation is mostly right-ventricular. Although few research have utilized MPI to evaluate right ventricular function in fetuses, most of these investigations have focused on left ventricular MPI. Furthermore, left ventricular MPI

may be included into conventional assessments of fetal well-being.

Therefore, we hypothesized that left ventricular Mod-MPI may be a useful tool for assessing fetal myocardial function in preeclamptic pregnancies. This study aimed to compare pregnant women with preeclampsia and gestational diabetes to healthy controls in order to determine the effects of fetal modified MPI.

2. Preeclampsia

Proteinuria, dysfunction of the mother's organs, or dysfunction of the uteroplacenta (such as fetal growth restriction (FGR) or angiogenesis imbalance) are the diagnostic criteria for preeclampsia, a complicated multisystem disease. The patient must have a history of normotension and experience hypertension suddenly during the course of the pregnancy (>20 weeks). (1).

The ISSHP categorizes preeclampsia as either preterm (birth occurs before 37 weeks of gestation), term (delivery occurs beyond 37 weeks of gestation), or postpartum preeclampsia. (2).

Preeclampsia is a hypertension disorder that affects 2-8% of pregnant women globally. This causes 9-26% of maternal mortality in countries with low incomes and 16% in countries with high incomes. (3). The combined effects of preeclampsia and eclampsia kill about 50,000 pregnant women annually. A higher maternal mortality rate is associated with preeclamptic pregnancies. The risk of fetal death is higher in preeclamptic pregnancies compared to non-preeclamptic pregnancies when there is fetal growth restriction (FGR) and placental abruption. (4).

• Symptom severity

- Severe conditions include a blood pressure reading over 160/110 mmHg together with another medical problem, such as HELLP syndrome (high blood pressure, increased liver enzymes, and low platelet count) or fetal growth restriction below the tenth percentile.
- This condition is considered moderate if the blood pressure is above 140/90 mm Hg and there is another medical problem, such as proteinuria (a ratio of 30 mg/mmol or higher for urine protein to creatinine, or an albumin to creatinine ratio of 8 mg/mmol or higher), or a 24-hour urine collection of 0.3 g/day or higher. (5).

- **Risk factors**

Preeclampsia has been associated with many well-documented risk factors. (Table 1).

- **Pathophysiology of preeclampsia**

In the two-stage model of preeclampsia, the first stage is placental failure leading to syncytiotrophoblast stress, and the second stage is the clinical manifestations in the mother. In the first stage of syncytiotrophoblast stress, symptoms include cell death, mitochondrial malfunction, oxidative stress, stress on the endoplasmic reticulum, and metabolic dysregulation. (Figure 1) (6).

Table (1) The ISSHP, ACOG, and NICE risk assessment checklists respectively ⁽¹⁾

Risk factor level	ISSHP	ACOG	NICE
	Preeclampsia in the past	History of preeclampsia	Preeclampsia History
	Renal illness that persists throughout time	Renal illness that persists over time	Renal illness that persists over time
	Persistent high blood pressure	Chronic hypertension	Chronic hypertension
Risk factor level	The metabolic syndrome	Type 2 diabetes	Mellitus diabetes
	APS or SLE	SLE or APS	SLE or APS
	Body mass index ≥ 30 kg/m ²	–	–
	Modified in vitro fertilization	–	–
	–	Multiple pregnancy	–
	My first pregnancy	First pregnancy	First pregnancy
	Age ≥ 40 years	Age ≥ 40 years	Age ≥ 35 years
	Pregnancy with several foetuses	–	–
	Previous abruption of the placenta	–	–
	Preceding stillbirth	–	–
	Past limitations on fetal growth	–	–
Risk factor level	–	Body mass index ≥ 35 kg/m ²	Body mass index ≥ 30 kg/m ²
	–	Inter-pregnancy interval >10 years	Inter-pregnancy interval >10 years
	–	Family history of pre-eclampsia	Family history of pre-eclampsia
	–	–	Black ethnicity
	–	–	Low socioeconomic status

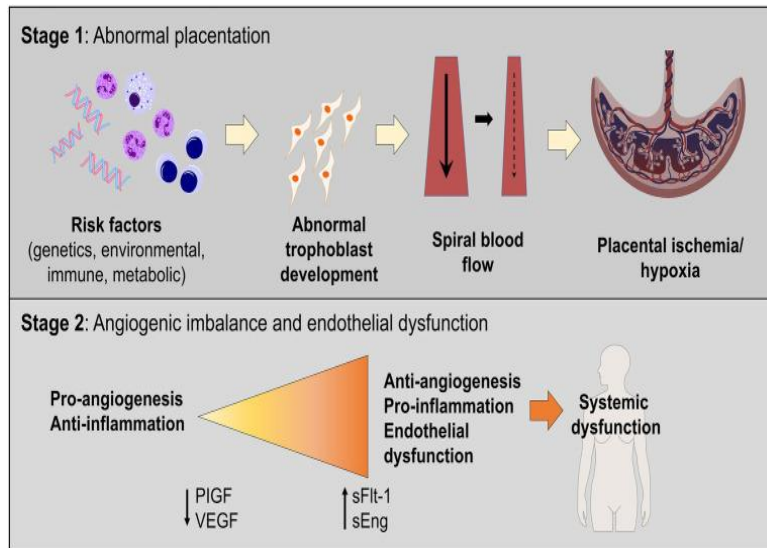


Fig. (1) The two-stage model of preeclampsia pathophysiology... In the first, preclinical stage, aberrant placentation causes soluble substances to be released into the mother's circulation, which in turn causes hypertension and systemic endothelial dysfunction in the second, clinical stage. ⁽⁷⁾

Under stress, the syncytiotrophoblast secretes a plethora of abnormal molecules into the mother's circulation, including as cytokines that promote inflammation, reactive oxygen species, extracellular vesicles, and compounds that inhibit angiogenesis. These conditions impact the endothelial function of women and worsen systemic multiorgan disease, which manifests as reduced vasodilation, systemic inflammation, and thrombosis (stage 2). ⁽⁸⁾

• **Impact of preeclampsia on fetal heart and systemic maternal complications:**

➤ **Effect of preeclampsia on fetal heart:**

The symptoms of a preeclamptic pregnancy include low blood flow to the placenta and an increase in the resistance of the umbilical cord. During this stage, the development of the heart is affected by the proliferation and differentiation of smooth muscle cells that surround the placental arteries. Impaired fetal cardiac function might be the result of an increased fetal cardiac afterload, which is brought about by an inflated placental vascular resistance. ⁽⁹⁾

Preload and foetal cardiac afterload are changed in PE, which might lead to changes in diastolic and systolic function. Systolic dysfunction, which occurs with a prolonged period of isovolumetric contraction, was believed to be the major component. Due to the low pressure, a greater contraction of the heart muscle is required to open the aortic valve in PE. ⁽¹⁰⁾

The inability to adjust to a higher volume and pressure load may cause arterial stiffness, whereas global diastolic dysfunction can cause left

ventricular failure. Additionally, after giving birth, they show signs of left ventricular remodeling, which becomes worse with age and the appearance of risk factors for cardiovascular disease, including thicker relative walls. ⁽¹¹⁾

In premature pulmonary embolism, the left ventricle is more likely to enlarge and malfunction. Therefore, it is hypothesized that prenatal exposure to PE increases the risk of cardiovascular disease (CVD), including arrhythmias, heart failure, coronary and peripheral artery disorders, and an increased likelihood of heart failure. ⁽¹²⁾

Alterations in the structure and function of the heart may be linked to prenatal hemodynamics in preeclampsia. Infants whose mothers have peripartum hemorrhage may be born with a small heart due to a combination of factors such as a high umbilical artery resistance, worldwide diastolic dysfunction, poor cardiac output, reduced cardiac reserve, and increased resistance to the circulatory sluggish output. ⁽¹¹⁾

Offspring exposed to mild to severe maternal PE also had an elevated incidence of pulmonary artery hypertension. Thus, vascular stiffness is elevated in the peripheral vascular system as well as the pulmonary system. ⁽¹³⁾

➤ **The systemic effects of preeclampsia on the mother:**

Complications that may arise from preeclampsia include eclampsia (seizures), hemorrhagic stroke, hemolysis, placental abruption, renal failure, pulmonary oedema, and the HELLP syndrome. ⁽¹⁴⁾

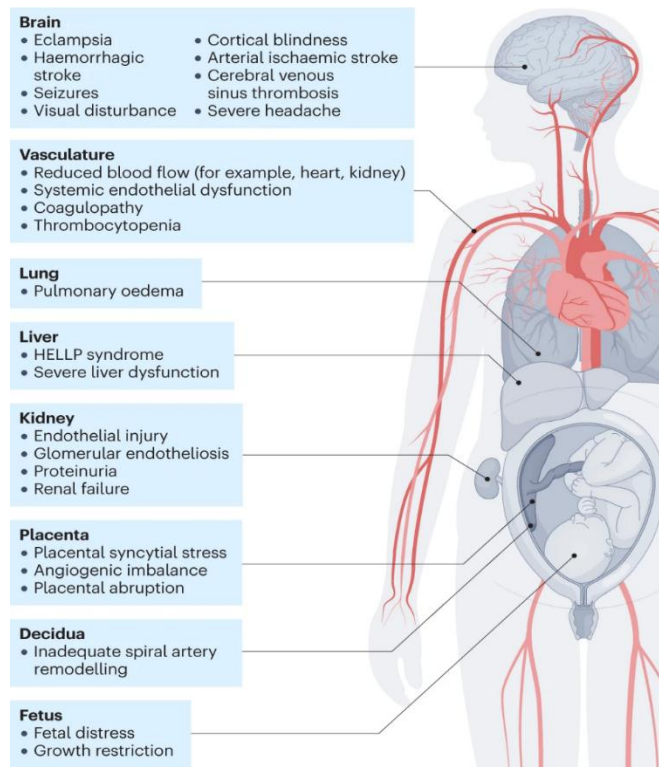


Fig. (2) Organs of the mother impacted by preeclampsia ⁽¹⁾

Diabetes mellitus during pregnancy (GDM)

When glucose intolerance of any severity begins during pregnancy or is first detected during pregnancy, it is referred to as gestational diabetes mellitus (GDM). There are two types of GDM: A1GDM and A2GDM. Diabetic gestational diabetes (GDM) or A1GDM is a kind of gestational diabetes that is treated with dietary treatment and does not need medication. Another side of the coin is A2GDM, which stands for gestational diabetes controlled with medication to achieve acceptable glycemic control. ⁽¹⁵⁾

Conventional methods of screening for gestational diabetes included reviewing the patient's medical history, obstetric results from the past, and any relatives with a history of type 2 diabetes. It served its purpose, yet it was inappropriate. About half of the pregnant women with GDM were missed by this screening strategy. Nearly all obstetricians in the US use the 50 g 1-hour oral glucose tolerance test to screen for gestational diabetes mellitus (GDM) during pregnancy. This method has been recommended for use since 1973 by a large-scale study. The United States Preventive Services Task

Force advised screening all pregnant women for gestational diabetes mellitus at 24 weeks of gestation in 2014. ⁽¹⁶⁾

• **Pathophysiology**

A hormone secreted by the placenta during pregnancy is known as the human placental lactogen. Its structure is similar to that of growth hormone, and it triggers crucial metabolic changes in the developing fetus to aid in the preservation of the fetal nutritional status. Changes and adjustments to the insulin receptors may be induced by this hormone. When glucose absorption in peripheral tissues decreases, it may be because of the following molecular variations: 1) Insulin receptor substrate-1 and phosphatidylinositol 3-kinase remodeling, 2) reduced tyrosine kinase phosphorylation, and 3) molecular changes to the beta-subunit insulin receptor. Fetal hyperglycemia occurs when maternal glucose levels are high enough to pass the placenta. In reaction to the high blood sugar, the fetal pancreas is activated. Insulin stimulates accelerated development of embryonic tissues due to its anabolic characteristics. ⁽¹⁷⁾

Table 2: Risk factors for gestational diabetes include ⁽¹⁸⁾:

Modifiable risk factors	<ul style="list-style-type: none"> • Being overweight, obese, or having a body mass index (BMI) that was higher before pregnancy • Metabolic syndrome and nutritional diet • Polycystic ovary syndrome (PCOS) • Preeclampsia • Other modifiable risk factors for gestational diabetes mellitus (GDM) include:
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	smoking, poor sleep hygiene, using antidepressants and psychotropic medications, and prolonged exposure to environmental psychological stress.
Non-modifiable risk factors	<ul style="list-style-type: none"> • Mothers who are 25–30 years old or older • Gravidity and parity: a woman's risk of gestational diabetes mellitus (GDM) may increase with each subsequent pregnancy and each subsequent delivery. • Hispanic, African-American, and Asian women are among the many racial and ethnic groups that have an elevated risk of gestational diabetes mellitus (GDM). • A history of high blood sugar in the family and heredity.

• **Differential diagnosis**
Differentiating between gestational diabetes and preexisting diabetes might be difficult since many women do not have the proper diabetes mellitus test prior to becoming pregnant. ⁽¹⁹⁾

• **Complications**
Both the mother and the unborn child are vulnerable to the difficulties that might arise from gestational diabetes. Some of the issues that may occur during pregnancy include large baby weight, low blood sugar, polycythemia, shoulder dystocia, high levels of bilirubin, respiratory distress syndrome in newborns, higher risk of death during pregnancy, and low calcium levels. Complications that might arise during pregnancy include high blood pressure, preeclampsia, an increased likelihood of developing

diabetes mellitus, and the need for a cesarean section. ⁽²⁰⁾

➤ **GDM and consequences on fetal heart and mother**

In addition to increasing the likelihood of problems during pregnancy for both mother and child, gestational diabetes mellitus also increases the likelihood of problems in the future for both parties. ⁽²¹⁾

➤ **GDM consequences on fetal heart**

The fetal heart is more likely to develop anatomical abnormalities, hypertrophy, and functional impairment when the mother has diabetes while she is pregnant. ⁽²²⁾

Major congenital heart defects in children born to moms with diabetes ⁽²³⁾.

Table (3) Types of major cardiac congenital anomalies in offspring of diabetic mothers are showing:

Cardiovascular system	
Isthmia ventricularis hypoplastica	
The acronyms AVSD and VSD	
Atresia of the tricuspid and mitral valves	
The left ventricle has two openings	
The right ventricle has two outlets.	
Great artery transposition	
The Expansion of Tetralogy	

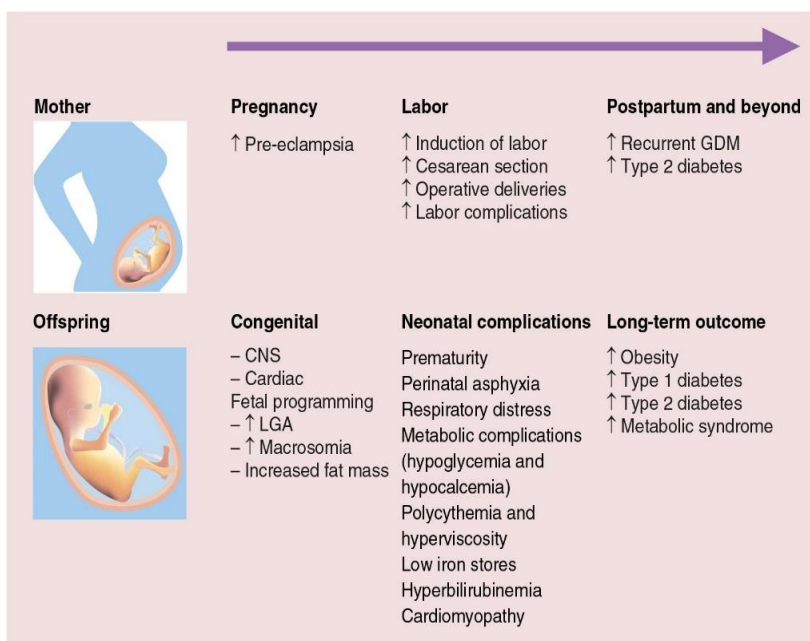


Fig. (3) Health effects of gestational diabetes mellitus on women and their children, both in the short and long term ⁽²⁶⁾

Babies whose moms with diabetes are at increased risk for cardiovascular defects such as hypertrophic cardiomyopathy. A characteristic of this abnormality is thickening of the interventricular septum that reaches the free wall of the ventricles.⁽²⁴⁾

Nine percent to fifty percent of pregnant women with gestational diabetes mellitus (GDM) also have fetal cardiac dysfunction and/or hypertrophic cardiomyopathy (HCM).⁽²⁵⁾

Fetal hyperinsulinemia in mothers with diabetes may set off the development of infantile hypertrophic cardiomyopathy. In this disorder, the cardiac muscle cells multiply and enlarge due to an increase in the hormone's affinity for the insulin receptors. This could lead to some visible variations in the inflow and outflow velocities of the baby's ventricles.⁽²⁵⁾

There is some indication that diastolic cardiac shortening velocities are increasing while left ventricular function is decreasing.⁽²⁷⁾

Some congenital cardiac defects that are more frequent in people with this condition include septal malformations, chronic truncus arteriosus, and transposition of the major arteries.⁽²⁸⁾

Changes in morphology and structure caused by diabetes in the mother may coexist with anomalies in fetal cardiac sonography that point to functional impairment. All of these functional changes—poor ventricular filling, a blocked outflow route, and dysfunction during systole and diastole—lead to an elevated heart rate and decreased overall myocardial performance.⁽²⁹⁾

Finally, increased fetal circulation, thickening ventricular walls, reduced diastolic function, and global ventricular function were some of the cardiac anatomical and functional abnormalities seen in GDM babies.⁽³⁰⁾

Measures of heart function include the Tei Index and the Modified Tei Index

In the last 30 years, foetal echocardiography has emerged as the gold standard for noninvasively assessing the structure, function, and hemodynamics of the fetal heart. Fetal echocardiography primarily aims to assess the heart function of the developing fetus.⁽³¹⁾

Usually, a screening fetal echocardiography will be done between the ages of 18 and 22 weeks throughout the pregnancy. Anatomical landmarks such as the foetal head and sagittal plane have been identified. The transducer is positioned so that it is perpendicular to the fetal sagittal plane, with the head perpendicular to the screen to the right. To see the foetal thorax in a cross-sectional plane, the transducer is then turned clockwise by 90 degrees. The foetus's organs are located on the left side, opposite the spine, as seen on the screen. After establishing the abdominal and cardiac situs, the next step is to find the cardiac axis and orientation in the transverse plane. Common cross-sectional views include those of the heart's four chambers, its left and right

ventricles, its blood vessels, and its trachea, which includes the ductal and aortic arches.⁽³²⁾

Functional cardiac evaluation using echocardiography is gaining popularity as a means to enhance newborn outcomes by guiding treatment and detecting mild myocardial abnormalities throughout development. The myocardial performance index (MPI) is a quantitative assessment that has shown to be an extremely sensitive indicator of dysfunction. It is generated from pulsed-wave Doppler and represents global myocardial function.⁽³³⁾

Originally introduced in 1995 by Tei et al., the myocardial performance index (MPI) measures⁽³⁴⁾ that people suffering from dilated cardiomyopathy get cardiac evaluations. During the ventricular filling phase, the first approach measured the time between the end of the A-wave and the start of the following E-wave to get the isovolumetric time (a). The aortic or pulmonary outflow tracts were used to assess the ejection time (b). By dividing (a—b) by b, the final MPI was calculated.

The Tei indicator, afterwards rechristened the MPI, is a pulsed-wave derived indicator that typically integrates evaluation of cardiac time intervals. It is defined as follows.⁽³⁵⁾

MPI is equal to the sum of the isovolumetric contraction time (ICT) and the isovolumetric relaxation time (IRT) divided by the ejection time (ET) minus 1.

In subsequent studies, MPI was suggested by several researchers as a feasible approach to estimate fetal cardiac adaptation changes throughout complex pregnancies. Nevertheless, the findings demonstrated a significant deviation from the standard reference values, likely caused by the absence of discernible landmarks in the Doppler waveforms used to determine the time-periods. It was proposed that a single Doppler waveform may be used to assess the left ventricle's MPI, which would solve this difficulty.⁽³⁶⁾

Friedman et al.⁽³⁶⁾ in 2003 suggested a different location for the Doppler sample volume, which allowed for the evaluation of the left ventricular MPI using just one Doppler waveform. Because the fetal heart's mitral input and aortic outflow passages were so close together, it was possible to measure both the isovolumetric period and the ejection time during the same cardiac cycle.

Doppler echoes, often called "clicks," appear as vertical stripes on a Doppler waveform as valve leaflets open and close. Raboisson et al. made further revisions to the left MPI calculation algorithm in 2003.⁽³⁷⁾ to improve the estimation of the time intervals for MPI computation, they advocated using the Doppler click of the opening of the aortic valve as a marker.

In 2005, **Hernandez-Andrade et al.**⁽³⁸⁾ presented the modified MPI (Mod-MPI), which uses the starting Doppler clicks of the aortic and mitral valves to determine the various time periods. The

repeatability of the index in fetal medicine was enhanced as a result of the considerable reduction in inter- and intra-observer variability. Within an apical four-chamber view of the foetal heart, the Doppler sample gate was positioned on the lateral wall of the ascending aorta, near the mitral valve, for the left Mod-MPI.

A noninvasive measure of global myocardial function, the fetal modified myocardial performance index (Mod-MPI) has been studied in fetal cardiology. It is a ratio of isovolumetric to ejection time cardiac time intervals, and its use in clinical assessments of fetal cardiac function is well-established for the left ventricular Mod-MPI.⁽³⁹⁾

For the purpose of studying fetal heart function in various conditions, including growth restriction, twin-twin transfusion syndrome, preeclampsia, intrahepatic cholestasis of pregnancy, adverse perinatal outcomes, and maternal diabetes, the Modified Myocardial Performance Index (Mod-MPI) is a dependable and practical tool.⁽⁴⁰⁾

Higher MPI values are related with ventricular dysfunction, which is often caused by an extended IRT. Many foetal diseases and disorders, including as preeclampsia and maternal diabetes, have been shown by the MPI to show foetal cardiac dysfunction.⁽⁴¹⁾

- **Preeclampsia and its effect on a tweaked MPI:**

Regardless of the presence or absence of growth restriction, the pre-eclamptic group exhibited higher MPI values when compared to the control group.⁽⁴²⁾

Chen et al.⁽⁴³⁾ discovered a significant disparity in the left MPIs between the control group and the group with pregnancy-induced hypertension syndrome..

Fetuses of preeclamptic mothers exhibited extended isovolumic relaxation durations and elevated left myocardial performance indices when compared with those of healthy mothers. The results suggest that the increase in fetal cardiac afterload in mild preeclampsia may have been the driving force behind the early subclinical changes in fetal systolic and diastolic cardiac function.⁽¹⁰⁾

Pregnancies with severe early onset preeclampsia considerably decrease fetal cardiac function, regardless of whether growth restriction is present and becomes worse with worsening grades of placental vascular resistance. The MPI has the ability to be included into standard foetal monitoring procedures.⁽⁴⁴⁾

Ultrasound and biochemical studies revealed structural and functional cardiac abnormalities in PE, including hypertrophy and enlargement of the heart, and elevated myocardial performance index, respectively.⁽⁴⁵⁾

- **Impact of maternal GDM on modified MPI:**

Left ventricular MPI is higher in fetuses of mothers with pre-gestational or poorly managed

diabetes compared to non-diabetic controls from the beginning of the first trimester until the end of the pregnancy. It has also been shown that, as compared to normal babies, gestational diabetics have abnormal foetal left Mod-MPI. The rise in IVRT was the primary factor that caused the MPI value to rise throughout pregnancy, although it was most pronounced in the third trimester.⁽⁴⁶⁾

It is possible that changes in myocardial compliance are associated with subclinical diastolic dysfunction and elevated left MPI. This suggests that gestational diabetes mellitus (GDM) could hinder ventricular diastolic functioning apart from abnormal fetal myocardial hypertrophy.⁽⁴⁶⁾

Fetuses whose mothers had diabetes showed consistently elevated levels of left ventricular MPI, suggesting that the disease had an impact on this fetal parameter. In a similar vein, the fetuses of diabetes moms had considerably higher levels of IRT and ICT when contrasted with the control group.⁽⁴⁷⁾

Fetuses of diabetes moms had a markedly elevated MPI, a measure of global heart function (systolic and diastolic). Preeclampsia and other placental-mediated diseases: the clinical relevance of a modified MPI for prognosis⁽⁴⁸⁾

Foetal and neonatal evidence of subclinical cardiac function impairment has been found in several research involving the children of pregnant women with preeclampsia. Preeclampsia in future generations may be more likely to develop cardiovascular complications due to early structural and functional alterations in the heart.⁽⁴⁹⁾

Maternal preeclampsia was associated with higher systolic and diastolic blood pressure in several studies compared to normotensive pregnancies. All of the people who took part in these studies were either young adults or in the midst of their teenage years.⁽⁵⁰⁾

Hypertensive pregnancies that delivered at 35 or 36 weeks of gestation were found to have a higher likelihood of having babies that were small for their gestational age (17.9% vs 1.7% [P \.05] and 33.3% vs 12.2% [P \.01] and 57.1% vs 34.5% [P \.05] and 33.3% vs 10.7% [P \.001] respectively) and of needing admission to the neonatal intensive care unit. The likelihood of neonatal intensive care unit admission was greater (25.6% vs 8.7%; P <.001) and the duration of neonatal stay was longer (3.9 vs 2.0 days; P <.001) in hypertensive pregnancies who gave birth at 37 weeks of gestation.⁽⁵¹⁾

Myocardial performance index is a trustworthy indicator that may detect early-stage, subclinical changes in heart function.⁽⁵²⁾

The prevalence of both DV anomalies and MPIs rises in tandem with the degree of growth restriction, and several studies have shown that MPI abnormalities appear long before vascular redistribution happens. According to these research, the degree of cardiac dysfunction is monitored, and it is very probable that this is the first quantitative

parameter to become abnormal in placental-mediated sickness. Despite initial concerns about the severity or stability of the placental-mediated sickness, a single high MPI may indicate the onset of difficulties later in the pregnancy, according to the research..⁽⁵³⁾.

In comparison to the control group, the preeclamptic group showed higher MPI values regardless of whether growth restriction was present or not. Fetal cardiac function is highly impaired in pregnancies with severe early onset preeclampsia, and this impairment worsens with increasing grades of placental vascular resistance; it occurs independently of the presence or absence of growth restriction..⁽⁴⁴⁾.

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