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# Interventricular Septal Thickness and Doppler Indices as Multiparametric Assessment of High-Risk Pregnancy and Their Relation to Fetal Outcome

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## ABSTRACT

**Background:** Basic ultrasound measurement is not enough for proper assessment for the high-risk pregnancy like gestational diabetes mellitus and preeclampsia.

**Objective:** This study aimed to add more parameters for evaluation of high-risk pregnancy including Doppler parameter and interventricular septal thickness, and their reflection on fetal outcome

**Patients and methods:** 75 pregnant women were presented between 28-38 weeks gestation. They were divided into three groups: Group I included 25 pregnant diabetic women, group II included 25 pregnant women with gestational diabetes mellitus (GDM) and preeclampsia, and group III included 25 normal pregnant women as a control group (NC). Fetal hemodynamic indices were measured to all included groups and represented as the resistance index (RI), pulsatility index (PI) of umbilical artery (UA), middle cerebral artery (MCA), and interventricular septal (IVS) thickness.

**Results:** The independent samples t-test showed that fetal weight, as well as the abdominal circumference (AC), was larger in GDM than in NC ($P < 0.05$) while were smaller in GDM with preeclampsia than in NC. Also, IVS thickness was larger in GDM than in NC ($P < 0.05$), while t-test showed that umbilical PI was higher in preeclampsia than in NC ($P < 0.05$) vice versa the MCA PI was lower in the preeclampsia than in NC ($P < 0.05$).

**Conclusion:** Doppler indices especially MCA and umbilical PI as well as the interventricular septal thickness in late pregnancy were helpful in the diagnosis and assessment of high-risk pregnancy as well as their follow-up and in turn they could be considered as an indicator of poor fetal outcome.

**Keywords:** Fetus, Gestational diabetes mellitus, Infant, Middle cerebral artery, Ultrasound, Umbilical artery.

## INTRODUCTION

Several factors can make pregnancy high risk, including for example diabetes mellitus (DM), pre-eclampsia (PE), rupture of membrane (ROM) as well as maternal age [(1)]. Clinical assessment of high-risk pregnancy including the biophysical profile and daily fetal movement does not offer a high stander level for assessment of fetal well-being with high sensitivity and specificity [(2)].

Antenatal screening of the uteroplacental flow by using Doppler indices of the umbilical, uterine arteries like pulsatile index, resistant index, or the presence of an early diastolic notch are used as a predictor of the antenatal complication like intrauterine growth restriction (IUGR) [(3)].

Decrease of the blood flow to fetal circulation leads to fetal brain hypoxia, which can be detected by an increase in the resistive index in the umbilical artery with a decrease in the middle cerebral artery resistive index, which is called "brain sparing" [(4, 5)].

Assessment of feto-placental vascular bed by using color Doppler gives information about feto-maternal circulation and its state, colour Doppler can assess the early abnormal pattern in the blood flow to the fetus, thus helping in the decision of the onset of the delivery, that leads to decrease of the maternal morbidity and mortality [(6)]. The fetal high insulin level due to changes in the diabetic mother metabolism leads to changes in the cardiomyocyte gene expression that in turn leads to malformation of the fetal heart not only at the level of the structure but also at the level of the cardiac function [(7)].

Asymmetrical increase of interventricular septal thickness is seen in the fetus with diabetic mother with an increase in the incidence in the fetus of mothers with insulin- dependent diabetes mellitus (IDDM) rather than insulin-independent DM (IIDM) [(8)].

The diagnosis of the increased interventricular thickness is documented by using Fetal echocardiography [(9)].

## PATIETNS AND METHODS

This observational prospective study was conducted from September 2020 until August 2021. The study included 75 pregnant women presented between 28-38 weeks gestation. They were divided into three groups: Group I (GDM group) included 25 pregnant women, group II (combined GDM with pre-eclampsia) included 25 pregnant women and group III (NC group) included 25 pregnant.

### Inclusion criteria:

Pregnant women with age ranging between 25–38 years, 3rd-trimester pregnant women of a single fetus between 28 weeks and 39-weeks gestation with GDM, and combined GDM with preeclampsia. Control group are 3rd-trimester pregnant women of a single fetus between 28 weeks and 39-weeks gestation with no risk factor, checked by measuring fasting plasma glucose (FPG) concentration that was less than 140 mg/dl and



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HbA1c below 6.5%. Regarding the GDM with preeclampsia, systolic pressure should exceed 140 mmHg and the diastolic more than 90 mmHg. The diagnostic thresholds for GDM were according to the ADA in 2016 during a two-hour oral glucose tolerance test (OGTT): glucose levels of 95, 140, and 120 mg/dl for fasting; one hour and two-hour respectively post 75 g glucose. All women investigated for fasting blood glucose level, two-hour postprandial blood glucose level, and HB A1c was done for the diabetic group

**Exclusion criteria:**

Pregnant women with twin or more gestation, gestational age more than 40 weeks, pregnant women within the 1st and 2nd trimester, pregnancy with any structural congenital fetal anomaly.

**Radiologic interventions:**

**2D ultrasound** through the transabdominal approach for all subject to assess the heart rate, amniotic fluid index, fetal basic measurement and to exclude the congenital anomalies. Measurement of the BPD start from the outer edge of the parietal bone near the transducer to the inner edge of the other side of the parietal bone at the level of the thalamus, the same plane for measuring the HC, the AC but measured from the outer layer of the skin in the area including the stomach and the spine. The FL was measured from the femur from end to end and EFW was calculated using Hadlock's formula [12, 13].

**Doppler Ultrasound** assessment included UA and middle cerebral artery (MCA). The umbilical artery was measured 5 cm from the placenta with a degree of beam less than 20°. Regarding the MCA, it was measured in the same plane of the BPD in the Sylvian fissure [14] with the same angle resembling the umbilical artery [15] [Figure 1].

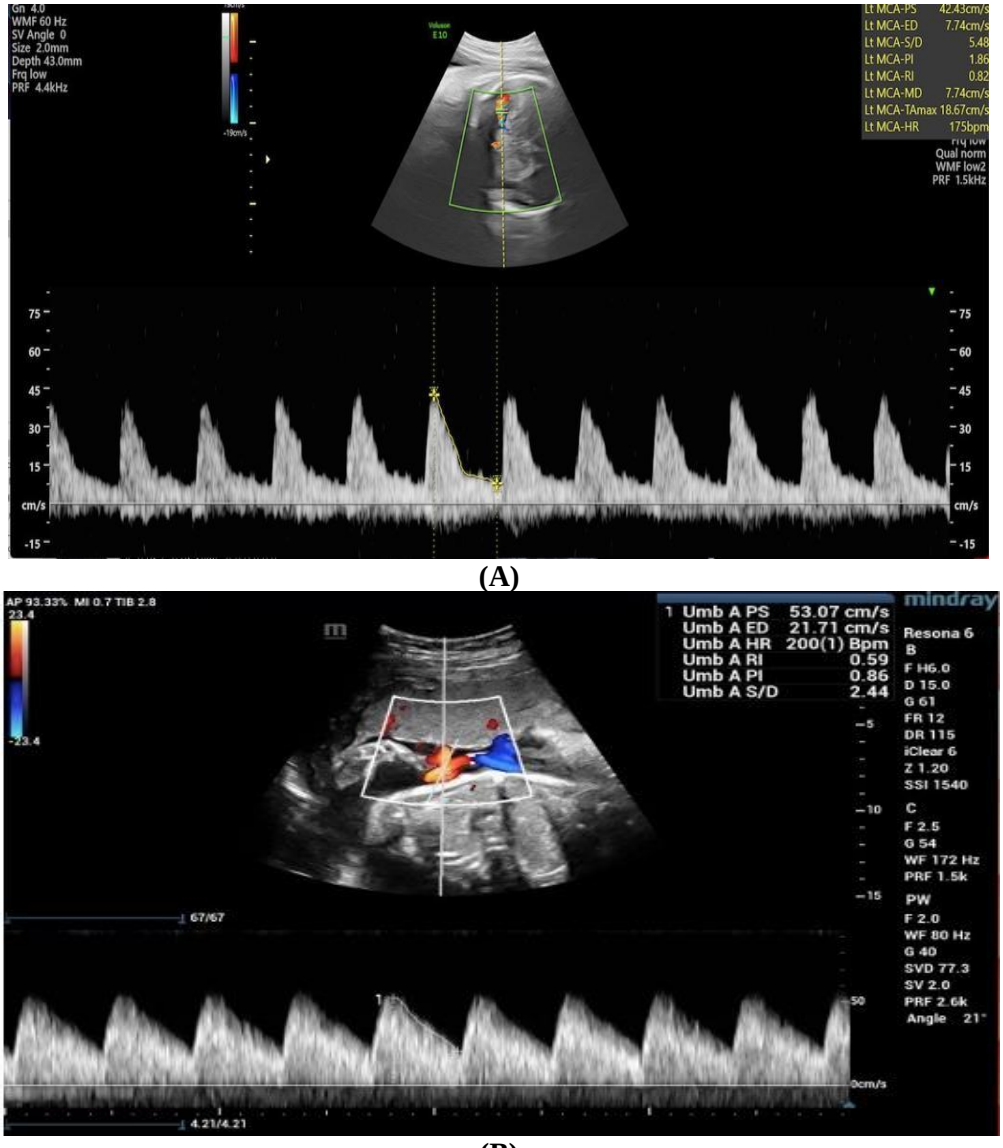
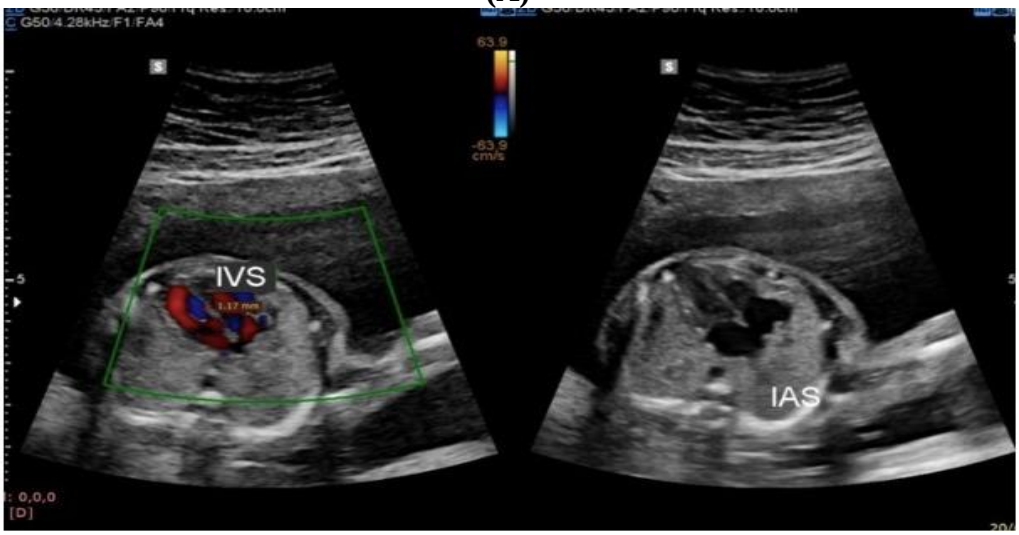



**Figure (1):** (A) Fetal Doppler ultrasound on the middle cerebral artery in Sylvain fissure that showed normal wave pattern. (B) Fetal Doppler ultrasound on umbilical artery near umbilicus that showed a normal wave pattern.

**FETAL ECHO Doppler** for Assessment of Interventricular septal thickness that was measured during diastole just inferior to the atrioventricular valves. [Figure 2].


**(A)**




**(B)**

**Figure (2):** Fetal ECHO that showed the normal thickness of IVS in a four-chamber view.

One senior sonographer underwent the sonography to eliminate any interpersonal errors, all measurements were taken twice, and the mean of each value was taken to decrease intrapersonal errors.

**Ethical consent:**

**This study was approved by the Research Ethics Committee of the Faculty of Medicine, Ain Shams University, Egypt on 16/03/2020. Reference number of approval: FWA000017585. FMASU R18/2020. A written informed consent was obtained by the parent or legal guardian of each patient. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

**Statistical analysis:**

Data were analyzed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). Measurement data were presented as mean ± standard deviation and count data were expressed as number and percentage (%). The independent samples t-test was used to compare the mean of continuous variables. The chi-square test was used as appropriate for comparing characteristics between two groups. Pearson's correlation coefficient was used to estimate the correlations among the hemodynamic indices (S/D, PI, and RI) of the fetal UA, MCA, IVS in late pregnancy and fetal weight. A difference of $P \leq 0.05$ is considered statistically significant.

**RESULTS**

The independent samples t-test showed that the fetal measurements including BPD, HC and FL were not significantly different between the two high-risk groups and NC ($P > 0.05$), while the AC was found to be significantly affected among the three groups as shown in table (1).

The independent samples t-test showed that the fetal Doppler measurements including umbilical RI, MCA RI, MCA PSV, Cerebro-placental ratio (MCAPI/UMBILICAL PI) were not significantly different between the two high-risk groups and NC ($P > 0.05$) as shown in table (1).

**Table (1):** Independent t-test in control cases and gestational diabetes among the selected gestational age

| | GDM (n=180) | NC (n=180) | P |
|---|---|---|---|
| **BPD** | **82.843** | **85.360** | **.286** |
| **HC** | **248.871** | **255.500** | **.421** |
| **AC** | **284.429** | **240.320** | **.000** * |
| **FL** | **68.143** | **66.280** | **.617** |
| **UA PI** | **1.0486 ± 0.23** | **9043 ± 0.23** | **.268** |
| **MCA PI** | **1.6614 ± 0.35** | **1.5386 ± 0.38** | **.546** |
| **IVS** | **0.5829 ± 0.2** | **0.2171 ± 0.5** | **.001** * |
| **fetal weight (gm)** | **2775 ± 133** | **2378.8 ± 103** | **.000** * |
| **Umbilical RI** | **0.568 ± 0.16** | **0.681 ± 0.2** | **0.121** |
| **MCA RI** | **0.77 ± 0.06** | **0.7529 ± 0.7** | **0.642** |
| **Cerebro-placental ratio** | **1.9486 ± 0.73** | **1.57 ± 0.58** | **0.3** |

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

The independent samples t-test showed that fetal weight, as well as the AC, were larger in GDM than in NC ($P < 0.05$) where the mean fetal weight in the GDM group was 2775 gm using Hadlock's formula and in the NC group was 2378.8 gm while it was smaller in GDM with preeclampsia than in NC ($P < 0.05$) where the mean fetal weight in the preeclampsia group was 1853.1429 gm and in the NC group was. 2119.2857 gm using Hadlock's formula. Also, in case of assessment of the IVS by independent samples t-test, it was larger in GDM than in NC ($P < 0.05$) where the mean IVS in the GDM group was 0.5829 mm and in NC group was 0.2171 mm.

While, MCA PI was lower in preeclampsia than in NC ($P < 0.05$) where the mean MCA PI in preeclampsia group was 1.108 and in NC group was 1.4257. Regarding the umbilical PI, it was higher in GDM with preeclampsia than in NC ($P < 0.05$) where the mean Umbilical PI in combined group was 1.1200 and in NC group was 0.8614 (Table 2).

**Table (2):** Independent t-test in control cases and combined gestational diabetes/preeclampsia among the selected gestational age

| | GDM with Preeclampsia (n=180) | NC (n=180) | P |
|---|---|---|---|
| **UA PI** | **1.1200 ± 0.10** | **0.86 ± 0.19** | **.010** * |
| **MCA PI** | **1.108 ± .09** | **1.4257 ± 0.41** | **.010** * |
| **IVS (mm)** | **0.4129 ± 0.2** | **0.4171 ± 0.5** | **.01** |
| **fetal weight** | **1853.1 ± 92 gm** | **2119.3 ± 128gm** | **.001*** |
| **AC** | **204.429** | **240.320** | **.000 *** |
| **Umbilical RI** | **0.7086 ± 0.06** | **0.6386 ± 0.1** | **0.164** |
| **MCA RI** | **0.818 ± 0.27** | **0.762 ± 0.09** | **0.171** |
| **MCA PSV** | **48.4 ± 11.4** | **40.78 ± 13.2** | **0 .269** |
| **Cerebro-placental ratio** | **1.6114± 0.421** | **1.544 ± 0.35** | **0.752** |

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

Pearson correlation showed a significant positive correlation between high-risk pregnancy and Doppler parameters with a postnatal outcome like neonate intensive care unit (NICU) admission for severe adult respiratory distress syndrome (ARDS), transient tachypnea with cyanosis, with values of .252, .302, and -.252 respectively , positive correlation between transient tachypnea with cyanosis and umbilical PI and IVS thickness with values of -.265 and .295 respectively, positive correlation between NICU admission for severe ARDS and MCA PI with a value of .317, a positive correlation between NICU admission for cardiomegaly and IVS thickness with a value of .510, positive correlation between mild tachypnea and umbilical PI with a value of -.355 and positive correlation between meconium aspiration and umbilical PI with value -.233 (Table 3).

**Table (3):** Pearson correlation (r) for the post-natal complication among all gestational age

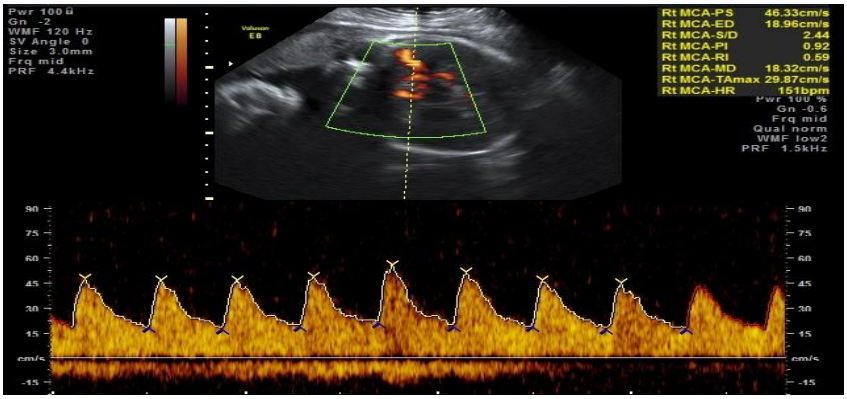
| | | Transient tachypnea | Transient tachypnea with cyanosis | NICU admission for severe ARDS | NICU admission for cardiomegaly | Mild tachypnea | Mild cyanosis | Meconium aspiration |
|---|---|---|---|---|---|---|---|---|
| **MCA PI** | r | -.097 | .157 | .317* | .079 | .047 | .135 | -.067 |
| | **P value** | .379 | .155 | .003 | .477 | .674 | .219 | .544 |
| **Umbilical PI** | **r** | .002 | -.265* | -.064 | .125 | -.355* | -.077 | -.233* |
| | **P value** | .988 | .015 | .560 | .257 | .001 | .489 | .033 |
| **fetal weight** | **r** | .018 | .088 | -.042 | .106 | .066 | -.127 | .185 |
| | **P value** | .873 | .425 | .703 | .337 | .551 | .248 | .092 |
| **IVS thickness** | **r** | -.010 | .295* | .168 | .510* | -.198 | -.133 | -.076 |
| | **P value** | .931 | .006 | .127 | .000 | .071 | .227 | .493 |
| **Risk Factor** | **r** | .185 | .252* | .302* | .192 | -.252* | -.156 | -.110 |
| | **P value** | .092 | .021 | .005 | .079 | .021 | .156 | .320 |

*significant

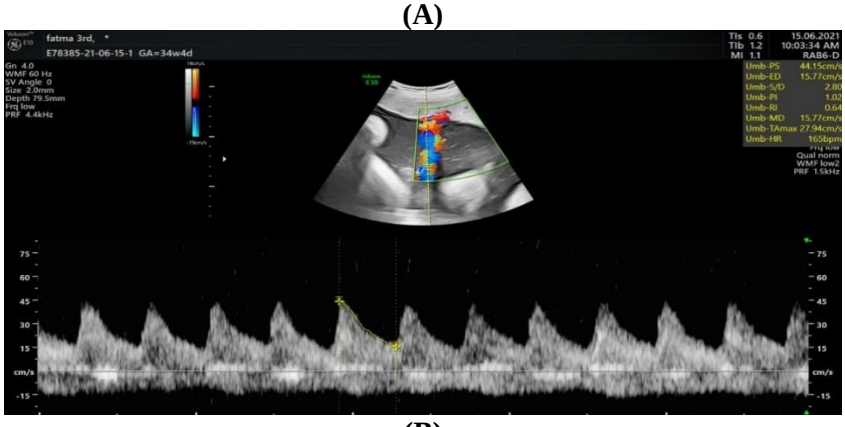
## DISCUSSION

High-risk pregnancy including DM and preeclampsia affect the fetus in utero including fetal growth affection either by increasing or decreasing fetal weight as well as bad fetal outcomes including post-natal NICU admission. The more combined risk factor will result in more affection of Doppler indices and IVS thickness, which in turn affect the fetal outcome. The most widely used calculation for fetal weight is Hadlock formula. Diabetic mothers with high glucose levels lead to increase fetal weight.

This study showed a negative correlation between the fetal weight and doppler parameters including MCA and umbilical artery RI and PI, while when accompanied with another risk factor like preeclampsia led to decrease of the fetal weight. Furthermore, in this study, there was a significant positive correlation between the microsomia and MCA and umbilical PI with non-significant correlation to the other Doppler parameters (Figure 3 a & b). Also, there was a significant correlation between DM and IVS thickness, which was best assessed in late 3rd trimester (Figure 4).




**(A)**



**(B)**

**Figure (3):** (A) Fetal Doppler ultrasound on the middle cerebral artery in Sylvain fissure showing abnormal wave pattern, (B) Fetal Doppler ultrasound on umbilical artery near umbilicus showing an abnormal wave pattern**.**


**Figure (4):** Fetal ECHO shows increase in thickness of IVS in four-chamber view.

High-risk pregnancy especially in combined form affects the fetal doppler that may lead to fetal anemia, which in turn shows a significant correlation with poor fetal outcome including NICU admission and ARDS. These results are consistent with **Verburg *et al.* (10)** study, which also showed that UA PI was negatively correlated with estimated fetal weight. Also, the same occurred with 106 pregnant women within study made by **Maruotti *et al.* (11)**. Moreover, **Liu *et al.* (12)** on 147 women with GDM and 124 NC showed that fetal weight parameters were larger in GDM than in NC ($P < 0.05$). and the fetal hemodynamic UA and MCA were lower ($P < 0.05$.

On the other hand, **Leung *et al.* (13)** found that UA-PI, MCA-PI, and MCA-Vmax were not useful in the prediction of abnormal pregnancy outcomes in GDM in a prospective study that was performed on 169 singleton GDM pregnancies.

The present results are in line with the results reported in a study by **Zanjani *et al.* (14)** study that was performed on 66 pregnant women, including 33 women with GDM and the others without it. Doppler parameters were recorded in UA as well as both right and left fetal MCAs. Although, all the measured Doppler parameters had higher values in GDM pregnancies, the differences were not significant between the two groups of study; except for the left fetal MCA-PI, which was significantly higher in the GDM group. They concluded that gestational diabetes may contribute to an elevated PI in the fetal MCA **(14)**. **Ovesen *et al.*(15)** studied the effect of GDM on maternal and fetal outcomes through a cohort study. The risk of preeclampsia, cesarean section (both planned and emergency), and shoulder dystocia was increased in women with GDM. The risk of thrombosis was increased in the GDM patients. The GDM women had an increased risk of giving birth to a macrosomic neonate. Low Apgar score was increased in the GDM.

## CONCLUSION

Doppler indices especially MCA and umbilical PI and interventricular septal thickness in late pregnancy were helpful in the diagnosis and assessment of high-risk pregnancy as well as their follow-up and in turn could be considered as an indicator of poor fetal outcome.

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

**Competing interests:** We have no competing interests to declare

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