Role of middle cerebral artery, umbilical artery resistance indices and middle cerebral artery to umbilical artery resistance index ratio in predicting unfavorable perinatal outcomes of normotensive and hypertensive diabetic pregnancies

Usama M. Fouda *, Mohamed M. Abou ElKassem, Shamel M. Hefny, Ahmed T. Hashem

Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Cairo, Egypt.
umfrfouda@yahoo.com

Abstract: Objective: To evaluate the role of middle cerebral artery (MCA), umbilical artery (UA)resistance indices (RI) and middle cerebral artery / umbilical artery resistance index ratio(MCA/UA RI) in predicting unfavorable perinatal outcomes in pregnancies complicated with diabetes mellitus. **Methods:** This prospective study included 96 women divided into 4 groups. Group 1 included 23 pregnant patients with preexisting diabetes, group 2 included 22 patients with gestational diabetes, group 3 included 24 diabetic pregnancies associated with hypertension and group 4 was a control group which included 27 patients with uncomplicated pregnancies. The umbilical artery and middle cerebral artery resistance indices were measured weekly starting from the 34th till the 38th week of pregnancy. **Results:** Abnormal UA RI (≥ 95th centile) had 78.57% sensitivity in detecting adverse perinatal outcomes in group 3 compared with 16.67 % and 0% sensitivity in group 1 and group 2 respectively. Abnormal MCA RI (≤ 5th centile) had 50% sensitivity in detecting adverse perinatal outcomes in group 3 compared with 0% sensitivity in groups 1 and 2. Abnormal MCA/UA RI (< 1) had 71.43 % sensitivity in detecting adverse perinatal outcomes in group 3 compared with 0 % sensitivity in groups 1 and 2. **Conclusion:** The abnormal UA RI, MCA RI and MCA/UA RI may be useful parameters in predicting adverse perinatal outcomes in diabetic pregnancies associated with hypertension. On the other hand, there were weak correlations between abnormal UA RI, MCA RI, MCA/UA RI and adverse perinatal outcomes of diabetic pregnancies not associated with hypertension. Therefore the results of the UA RI, MCA RI and MCA/UA RI should be interpreted with caution in the management of diabetic pregnancies, especially those not associated with hypertension, as adverse perinatal outcomes frequently occur in patients with normal Doppler indices.

[Usama M. Fouda, Mohamed M. Abou ElKassem, Shamel M. Hefny and Ahmed T. Hashem. **Role of middle cerebral artery, umbilical artery resistance indices and middle cerebral artery to umbilical artery resistance index ratio in predicting unfavorable perinatal outcomes of normotensive and hypertensive diabetic pregnancies.** *Life Sci. J.* 2013;10(3):2371-2377]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 345

Keywords: Diabetes mellitus, hypertension, Doppler ultrasound, Resistance index, Pregnancy

1. Introduction

Diabetes mellitus (DM) is a common medical disorder which complicates 7 % of all pregnancies **(1).** The prevalence of diagnosed diabetes among adults has increased from 4.9% in 1990 to 6.9% in 1999 **(2).** It is expected that the incidence of diabetes mellitus will increase by another 165% by 2050. This increase in the prevalence of diabetes (especially in young population) will consequently increase the prevalence of diabetic pregnancies. Diabetes with pregnancy leads to an increase in maternal and fetal complications such as preeclampsia, prematurity, malformations, macrosomia and perinatal morbidity and mortality. Although, the rates of perinatal mortality and morbidity associated with diabetic pregnancies have shown a progressive decline(mainly due to better preconceptional, antenatal, and neonatal care**),** these rates are still higher than that of the general pregnant population **(3)**.

During the past three decades, the protocols of antepartum fetal surveillance(non stress test, contraction stress test and Doppler) for high risk pregnancies became a part of routine obstetric practice. Although several studies showed that Doppler ultrasound can be used to assess fetal wellbeing in high-risk pregnancies complicated with chronic placental insufficiency, such as in pregnancies complicated with preeclampsia and intrauterine growth restriction. It remains uncertain whether Doppler ultrasound can be used to monitor pregnancies complicated with diabetes mellitus especially in the absence of hypertension or fetal growth restriction**(4,5)**.

The purpose of this study was to evaluate the role of middle cerebral artery (MCA), umbilical artery (UA) resistance indices (RI) and middle cerebral artery/ umbilical artery resistance index ratio (MCA/UA RI) in predicting unfavorable perinatal outcomes in pregnancies complicated with diabetes mellitus.

2. Patients and methods

This prospective study included 82 diabetic pregnancies and 30 uncomplicated pregnancies. The

patients were randomly selected from the antenatal clinic of Obstetrics and Gynecology department, Cairo University. The institutional ethics committee approved the study and informed consents were obtained from the patients.

In our institution, 75 gram oral glucose tolerance test (OGTT) was recommended for high risk women after the first antenatal visit. High risk women included those with maternal age above 35 years, obesity, family history of diabetes mellitus, glucosuria, past history of gestational diabetes, infant macrosomia and unexplained stillbirth.If the gestational diabetes was not diagnosed, blood glucose testing was repeated at 28 weeks or if the patient presented with symptoms or signs of hyperglycemia. The low-risk women underwent 75 mg OGTT at 28 weeks. Patients with two or more abnormal values of blood glucose level (fasting > 95 mg/dl, 1 hour > 180 mg/dl, 2 hours > 155 mg/dl) were considered as having gestational diabetes mellitus according to the American diabetes association criteria**(6)**. The following criteria were used in the diagnosis of diabetes mellitus;fasting plasma glucose level at or above 126 mg/dL, plasma glucose at or above 200 mg/dL two hours after a 75 g oral glucose load as in a glucose tolerance test, symptoms of hyperglycemia and casual plasma glucose at or above 200 mg/dL **(7)**.

The duration of pregnancy was determined from the last normal menstrual period, and confirmed by ultrasonographic biometry at 12-20 weeks. Chronic hypertension was defined as a blood pressure equal or more 140/90 mm Hg before 20 completed weeks of gestation. The diagnosis of gestational hypertension was made in pregnant women whose blood pressure reached 140/ 90 mmHg or greater for the first time during the second half of pregnancy but in whom proteinuria did not developed. Preeclampsia was diagnosed in pregnant women who were normotensive during early pregnancy, but later on demonstrated elevated blood pressure (140/90 mm Hg or more) and proteinuria (300 mg /24 h or more)**(8).**

The exclusion criteria were diabetic patients with ultrasound examination done more than one week before delivery, diabetic vasculopathy, preexisting medical conditions, such as renal disease and connective tissue disease, women who were unsure of the date of their last menstrual period, multiple gestation,major fetal abnormalities and absence of end diastolic waveform or reverse waveform.

Ultrasound and Doppler studies were carried out to determine gestational age, estimated fetal weight and biophysical profile. The umbilical and middle cerebral resistance index Doppler studies were performed weekly starting from the 34th till the 38th week of gestation. Intrauterine growth retardation (IUGR) was defined as estimated fetal weight of less than the 10th percentile for gestational age. Large for gestational age was defined as estimated fetal weight of more than the 90th percentile for gestational age. The ultrasound machine used was GE Voluson 73, with a Doppler unit and a 3.5 MHz convex linear probe. The output power of 50 mw/cm^2 was used and the high-pass filter was set to 100 Hz. Umbilical artery resistance index was estimated on a free loop of cord. For measurements of the middle cerebral artery resistance index, an axial view of the fetal head was obtained at the level of the cerebral peduncles. Color Doppler was used to visualize the circle of Willis. The Doppler sample volume was placed within 1 cm of the origin of the middle cerebral artery that was easily identified as a major branch running in anterolateral direction from the circle of Willis towards the lateral edge of the orbit **(9).** Waveforms of good quality were collected and analyzed in the absence of fetal breathing movements (to eliminate the effect fetal breathing on Doppler results). On average, three separate readings were performed and the mean value was recorded. For the waveform analysis, maximum and minimum values of the velocity waveforms on the frozen images were measured by use of electronic calipers of the machine. The Pourcelot resistance index (systole-diastole/diastole) was calculated by a built-in microcomputer (**10**). The Doppler indices within one week before delivery were included in the final analysis.

Adverse perinatal outcomes were defined as pregnancies with one or more of the following: caesarean section for non-reassuring cardiotocography, fetal acidaemia at delivery(pH < 7.2), 5-min Apgar of less than 7 or perinatal death. Abnormal Doppler indices were, umbilical artery resistance index of 95th centile or higher for gestation, middle cerebral artery resistance index of 5th centile or lower for gestation and MCA / UA RI ratio less than 1. During the study period, absence of or reversed end diastolic flow was an indication for early delivery. If the end diastolic flow was positive, the decision for delivery was not made only on the Doppler finding.

Statistical Methods

Data were statistically described in terms of range, mean ± standard deviation (SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Kruskal Wallis analysis of variance (ANOVA) test with Mann Whitney *U* test for independent samples as posthoc multiple 2-group comparisons. For comparing categorical data, Chi

square (χ^2) test was performed. Yates correction equation was used instead when the expected frequency was less than 5. Accuracy was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value, the likelihood ratio of a positive test and the likelihood ratio of a negative test. A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs, Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

A total of 112 women were recruited for the study. Sixteen women were lost to follow up and were excluded from final analysis. A total of 96 women were included in the final analysis, of which 69 were diabetics and 27 were non diabetics. The women were divided into four groups. Group 1 included 23 pregnant patients with preexisting diabetes mellitus, group 2 included 22 patients with gestational diabetes, group 3 included 24 diabetic pregnancies associated with hypertension and group 4 was a control group which included 27 patients with uncomplicated pregnancies.

The mean age, gravidity and parity were similar in the four groups. In group 1, eighteen patients had type1 DM and 5 patients had type2 DM.In group 3,fourteen patients had mild preeclampsia, two patients had severe preeclampsia, three patients had gestation hypertension and five patients had chronic hypertension. All the diabetic patients were on insulin therapy **(Table 1)**.

Table (1): Patients` characteristics and perinatal outcomes

	Preexisting diabetes (n=23) Group 1	Gestational diabetes (n=22) Group 2	Diabetes & hypertension (n=24) Group 3	Uncomplicated pregnancies (n=27) Group 4	*P* value G1 Vs G4	*P* value G2 Vs G4	*P* value G3 Vs G4
Age	26.35±2.6	26.32±3.1	26.21±2.5	25.96±2.18	0.52	0.85	0.52
Parity	2.52±1.16	2.59±1.14	2.33±1.09	2.65±0.87	0.72	0.89	0.45
Gravidity	3.61±1.27	3.68±1.43	3.42±1.44	3.56±1.12	0.97	0.68	0.58
Gestational age at delivery	37.21±0.75	37.72±0.92	36.65±0.77	37.69±0.75	0.03	0.85	0.0001
HgA1c (%)	5.66±0.8	5.1±0.6	5.77±0.79	n/a	n/a	n/a	n/a
Patients with HgA1c >6.5 %	5	0	5	n/a	n/a	n/a	n/a
Birth weight (grams)	3136±218	3106±218	2431±573	2861±152	0.0001	0.0001	0.005
Birth weight<10th percentile	0	0	8	0	n/a	n/a	0.004
Birth weight >90th percentile	4	3	0	0	0.083	0.167	n/a
Adverse perinatal outcomes	6	3	14	1	0.062	0.460	0.0001
C.S due to non reassuring CTG	1	2	6	1	0.908	0.855	0.072
Fetal acidaemia at delivery	1	1	6	0	0.935	0.917	0.020
Apgar score< 7 at 5th min	3	2	10	0	0.181	0.382	0.0007
Perinatal death	0	0	1	0	n/a	n/a	0.953
Stay in NICU>7 days	2	2	7	0	0.401	0.382	0.009

Values are expressed as mean ±SD, C.S = Caesarean section, NICU= neonatal intensive care unit, CTG= Cardiotocography

The birth weight was higher in groups 1 and 2 than in group 4. On the other hand, birth weight was lower in group 3 than in group 4. Eight fetuses in group 3 had birth weight less than the 10th percentile. Four fetuses in group 1 and three fetuses in group 2 had birth weight more than 90th percentile. Adverse perinatal outcomes were more frequent in group 3 (58.33%) compared with group 1 (26.08%) and group 2 (13.63%)**.** The mean HgA1c levels in the three diabetic groups were less than 6.5%. HgA1c was significantly lower in gestational diabetes group compared with the other two diabetic groups. Five patients in group1 and five patients in group 3 had HgA1c more than 6.5% **(Table 1).**There was no significant difference in HgA1c in diabetic patients with or without umbilical artery resistance index≥ 95th percentile (5.48±0.64 Vs 5.55±0.82, *P* value= 0.84).

There was no significant difference in the middle cerebral artery resistance index between the three diabetic groups and the control group.No significant difference in umbilical artery resistance index was detected in patients in groups 1 and 2 compared with patients in the control group. Umbilical artery resistance index was significantly higher in group 3 compared with the control group. Abnormal MCA/UA RI was detected in 11 out of 24 patients in group 3.None of the patients in groups 1 and 2 had abnormal MCA/UA RI.There were no patients with absent or reverse diastolic flow **(Table 2)**.

Table (2): Doppler indices of diabetic pregnancies and normal pregnancies							
	Preexisting diabetes (n=23) Group1	Gestational diabetes (n=22) Group2	Diabetes & hypertension (n=24) Group 3	Uncomplicated pregnancies (n=27) Group 4	*P* value		
					G1 Vs G4	G2 Vs G4	G3 Vs G4
UA RI	0.62±0.075	0.61±0.075	0.71±0.09	0.60±0.06	0.48	0.71	0.0001
MCA RI	0.79±0.053	0.8±0.052	0.76±0.09	0.79±0.05	0.47	0.26	0.68
MCA/UA RI<1	0	0	11	0	n/a	n/a	0.0003
Values are expressed as mean ± SD, UA= umbilical artery, MCA= middle cerebral artery, RI=resistance index							

Fourteen patients in group 3 had abnormal UA RI compared with three patients in group 1 and two patients in group 2. Abnormal UA RI had 78.57% sensitivity in detecting adverse perinatal outcomes in group 3 compared with 16.67 % and 0% sensitivity in group 1 and group 2 respectively. In group 3, 78.57% of patients with abnormal UA RI had adverse perinatal outcomes **(Table3).**

Table (3): Predictive value of UA RI for adverse perinatal outcomes			
	Preexisting diabetes (n=23) Group1	Gestational diabetes (n=22) Group2	Diabetes & hypertension (n=24) Group3
Normal; Abnormal UA RI	20;3	20;2	10;14
Percentage of adverse perinatal outcomes • **Normal Doppler (%)** • **Abnormal Doppler (%)**	 5;20(25%) 1;3(33.33%)	 3;20(15%) 0;2(0%)	 3;10(30%) 11;14(78.57%)
Sensitivity (%)	16.67%	0%	78.57%
Specificity (%)	88.24%	89. 47%	70%
Likelihood ratio for positive test	1.42	0.00	2.62
Likelihood ratio for negative test	0.94	1.12	0.31
Positive predictive value	33.33%	0%	78.57%
Negative predictive value	75%	85%	70%
UA= umbilical artery,RI=resistance index			

Eight patients in group 3 had abnormal MCA RI compared with one patient in group 1 and one patient in group 2. In group 3, abnormal MCA RI had sensitivity of 50% in detecting adverse perinatal outcomes in group 3 compared with 0 % sensitivity in groups 1 and 2.In group 3, 87.5% of patients with abnormal MCA RI had adverse perinatal outcomes. None of the patients in groups 1 and 2 with adverse perinatal outcomes had abnormal MCA RI. On the other hand, in group 3, 50 % of patients with adverse perinatal outcomes had abnormal MCA RI **(Table4).**

Table (4): Predictive value of MCA RI for adverse perinatal outcomes			
	Preexisting diabetes (n=23) Group1	Gestational diabetes (n=22) Group2	Diabetes & hypertension (n=24) Group3
Normal; abnormal MCA RI	22;1	21;1	16;8
Percentage of adverse perinatal outcomes • **Normal Doppler(%)** • **Abnormal Doppler(%)**	6;22(27.27%) 0;1(0%)	3;21(14.28%) 0;1(0%)	7;16(43.75%) 7;8(87.5%)
Sensitivity(%)	0%	0%	50%
Specificity(%)	94.12%	94.74%	90%
Likelihood ratio for positive test	0	0	5.00
Likelihood ratio for negative test	1.06	1.06	0.56
Positive predictive value	0%	0%	87.5%
Negative predictive value	72.73%	85.71%	56.25%
MCA= middle cerebral artery, RI=resistance index			

Eleven patients in group 3 had abnormal MCA/UA RI compared with no patients in groups 1 and 2. In group 3, abnormal MCA/UA RI had 71.43 % sensitivity in detecting adverse perinatal outcomes in group 3 compared with 0 % sensitivity in groups 1 and 2.In group 3, 90.91 % of patients with abnormal MCA/UA RI had adverse perinatal outcomes. None of the patients in groups 1 and 2 with adverse perinatal outcomes had abnormal MCA /UA RI. On the other hand, in group 3, 71.43% of patients with adverse perinatal outcomes had abnormal MCA/UI RI **(Table 5).**

Table (5): Predictive value of MCA/UA RI for adverse perinatal outcomes

	Preexisting diabetes (n=23) Group1	**Gestational diabetes (n=22) Group2**	**Diabetes & hypertension (n=24) Group3**
Normal; abnormal MCA/UA RI	23;0	22;0	13;11
Percentage of adverse perinatal outcomes • **Normal Doppler(%)** • **Abnormal Doppler(%)**	6;23(26.08%) 0;0(0%)	3;22(13.63%) 0;0(0%)	4;13(30.63%) 10;11(90.91%)
Sensitivity(%)	0%	0%	71.43%
Specificity(%)	100%	100%	90%
Likelihood ratio for positive test	n/a	n/a	7.14
Likelihood ratio for negative test	1.00	1.00	0.32
Positive predictive value	n/a	n/a	90.91%
Negative predictive value	73.91%	86.36%	69.23%
MCA= middle cerebral artery, UA= umbilical artery,RI=resistance index			

4.Discussion

The results of our study revealed that there was no significant difference in HgA1c in diabetic patients with and without umbilical artery resistance index≥ 95th centile. This indicates that the fetoplacental circulation in diabetic pregnancies was essentially unchanged, except in pregnancies complicated by hypertension. The results of our study are in agree with several studies which demonstrated normal Doppler indices in the uteroplacental circulation in diabetic pregnancies compared with normal pregnancies, except in cases with concomitant preeclampsia or intrauterine growth restriction**(11,12).**

The main cause of the increase in umbilical–placental resistance in growth-retarded fetus or hypertensive disorders with pregnancy is the obliteration of the small placental arteries within the placental vasculature **(13).**Several vascular changes have been detected in the placentas of gestational diabetic mothers, such as the narrowing of the lumen and changes in the syncytiotrophoblast and greater prevalence of fetal and placental vascular thrombosis **(14). Saldeen *et al.*,** reported that the conversion of arachidonic acid into prostaglandins is more increased in the placentas of diabetic pregnant women than in those of healthy pregnant subjects.Hyperglycemia results in increased transformation of arachidonic acid into thromboxane (TxA2) more than prostacyclin (PGI2), resulting in vasoconstriction of placental vascular bed which consequently increase the resistance in the uterine artery**(15)**. On the other hand, **Gelis *et al.*,** suggested that the relatively large placentas in diabetic pregnancies might have more tertiary stem villi and small arterial channels that give rise to reduced flow resistance**(16).**

Doppler ultrasound is commonly used to assess the fetal wellbeing in high-risk pregnancies. A meta-analysis on the use of Doppler ultrasound in high-risk pregnancies showed a significant reduction in perinatal deaths (risk ratio (RR) 0.71, 95% confidence interval (CI) 0.52 to 0.98, 16 studies, 10,225 babies, 1.2% versus 1.7 %, numbers needed to treat = 203; 95%CI 103 to 4352). There were also fewer inductions of labour (average RR 0.89, 95% CI 0.80 to 0.99, 10 studies, 5633 women, random effects) and fewer caesarean sections (RR 0.90, 95% CI 0.84 to 0.97, 14 studies, 7918 women**) (17).**

There are controversial reports on the use of Doppler ultrasound indices for assessment of fetal well-being in diabetic pregnancies. The majority of studies revealed that it is not useful for the assessment of fetal wellbeing. Only few studies have revealed that the abnormal UA RI(i.e. ≥ 95thpercentile) was an indicator of adverse perinatal outcomes **(4,5).**

In our study, abnormal UA RI had 78.57% sensitivity in detecting adverse perinatal outcomes in group 3 compared with 16.67 % and 0% sensitivity in group 1 and group 2 respectively. Abnormal MCA RI had 50% sensitivity in detecting adverse perinatal

outcomes in group 3 compared with 0% sensitivity in groups 1 and 2. In group 3, 78.57 % of patients with elevated UA RI had adverse perinatal outcomes. On comparing our results with other studies, **Tan *et al.,*** measured the RI of the umbilical artery weekly in 50 randomly selected diabetic mothers and a 50 non-diabetic pregnancies.They reported that there was no difference in the number of patients with abnormal umbilical artery resistance index between both groups.They reported that the majority of patients with abnormal fetal outcome had normal RI **(18).**

In a retrospective study, **Wong *et al.,*** evaluated the pulsatility index (PI) of the uterine artery in 104 pregnancies with preexisting diabetes at 28, 32,36,38 weeks gestation. They reported that 71% of pregnancies with abnormal Doppler studies had adverse perinatal outcomes. The sensitivity was 35%, specificity was 94%, positive predictive value was 80%, and negative predictive value was 68%. Only 30% of the women with adverse perinatal outcomes in this study had abnormal umbilical artery Doppler flow. They concluded that Doppler velocimetry was not a good predictor of adverse outcomes in diabetic pregnancies**(5). Bracero *et al.,*** examined umbilical artery Doppler velocimetry and glycemic control in the 227 patients with diabetes and concluded that an elevated umbilical S:D ratio and an abnormal glycosylated hemoglobin was associated with adverse pregnancy outcomes**(4).**

In the current study**,** eight patients in group 3 had abnormal MCA RI(i.e. $\leq 5^{th}$ percentile), compared with one patient in group 1 and one patient in group 2. In group 3, abnormal MCA RI had 50% sensitivity in detecting adverse perinatal outcomes in group 3 compared with sensitivity of 0 % in groups 1 and 2.In group 3, 87.5% of patients abnormal MCA RI had adverse perinatal outcomes**.** MCA/UA RI was less than 1 in 45.83 % of patients in group 3 and in no patients in groups 1 and 2. Abnormal MCA/UA RI had 71.43 % sensitivity in detecting adverse perinatal outcomes in group 3 compared with 0 % sensitivity in groups 1 and 2. In group 3,90.91% of patients with abnormal MCA/UA RI had adverse perinatal outcomes.

In normal pregnancies the diastolic component in the umbilical arteries is higher than in the cerebral arteries at any gestational age. Therefore, the placental resistance remains lower than the cerebro-vascular resistance and the cerebro-placental ratio is greater than 1. The index becomes less than 1 if there is an abnormal increase in the blood flow to the brain **(19).** Experimental studies have shown that the fetus can redistribute blood flow during chronic hypoxia, causing an increase in blood flow to the vital organs (brain, adrenal glands and myocardium)**(20).**The redistribution of circulation to the brain can be detected 2 to 3 weeks before the development of extreme changes of umbilical blood flow and the appearance of late deceleration on fetal heart rate tracing (**21**). Several reports suggest that the MCA/UA ratio Doppler indices appear to be a better predictor of unfavorable pregnancy outcome than are middle cerebral artery or umbilical artery indices separately(**22)**.The reported sensitivity of the MCA/UA ratio for prediction of unfavorable pregnancy outcome has varied from 40% to 88% **(21-23)**. MCA/UA ratio reflects not only the circulatory insufficiency of the umbilical velocimetry of the placenta manifested by alterations in the umbilical artery RI but also the adaptative changes resulting in modifications of the middle cerebral artery RI (**23).**

There are a number of explanations for the weak correlations between abnormal UA RI, MCA RI and MCA/UA RI and adverse perinatal outcomes of diabetic pregnancies not associated with hypertension. The pathophysiology of diabetes mellitus with pregnancy resulting in abnormal pregnancy outcome is poorly understood and likely to be multifactorial. It has been postulated that fetal hypoxia, fetal lactic academia (even in absence of hypoxia, due reduced capacity for oxidative metabolism), altered maternal and /or fetal metabolism, hypokalemia induced by hyperinsulinaemia are related to adverse perinatal outcomes in diabetic pregnancies**(11,24).** Fetal hypoxia in diabetic pregnancies may not be related only to placental insufficiency. Several theories have been postulated to explain causes of fetal hypoxia in diabetic pregnancies**(24)**. **Björk and Persson** suggested that the change in the structure of basement membrane of chorionic villi in diabetic pregnancies is the cause of decrease oxygen transfer and fetal hypoxia **(25)**. **Shelly *et al.,*** suggested that hyperinsulinaemia causes an increase in fetal oxygen consumption and a decrease in arterial oxygen levels**(26).**

In conclusion, the data presented in this study revealed that the abnormal UA RI, MCA RI and MCA/UA RI may be useful parameters in predicting adverse perinatal outcomes in diabetic pregnancies associated with hypertension. On the other hand, there were weak correlations between abnormal UA RI, MCA RI, MCA/UA RI and adverse perinatal outcomes of diabetic pregnancies not associated with hypertension. Therefore the results of the UA RI, MCA RI and MCA/UA RI should be interpreted with caution in the management of diabetic pregnancies, especially those not associated with hypertension, as adverse perinatal outcomes frequently occur in patients with normal Doppler indices.

Competing interests:

The authors declare that they have no competing interests.

Corresponding author:
Usama M. Fouda,
Department of Obstetrics and Gynecology, Faculty of Medicine,Cairo university.
E-mail: umfrfouda@yahoo.com

References

1. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2004; 27(Suppl 1): S88–S90.
2. Reece EA. The fetal and maternal consequences of gestational diabetes mellitus. J Matern Fetal Neonatal Med. 2010;23(3):199-203.
3. Reece EA. Diabetes-induced birth defects: what do we know? What can we do? Curr Diab Rep. 2012;12(1):24-32.
4. Bracero LA, Figueroa R, Byrne DW, Han HJ. Comparison of umbilical Doppler velocimetry, nonstress testing, and biophysical profile in pregnancies complicated by diabetes. J Ultrasound Med. 1996; 15: 301–308.
5. Wong SF, Chan FY, Cincotta RB, McIntyre DH, Stone M. Use of umbilical artery Doppler velocimetry in the monitoring of pregnancy in women with pre-existing diabetes. Aust N Z J Obstet Gynaecol.2003; 43(4): 302-6.
6. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2000;23(Suppl. 1):S77–S79.
7. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998;15(7):539-53.
8. Ozeren M, Dinç H, Ekmen U, Senekayli C, Aydemir V. Umbilical and middle cerebral artery Doppler indices in patients with preeclampsia. Eur J Obstet Gynecol Reprod Biol. 1999;82(1):11-6.
9. Simanaviciute D, Gudmundsson S. Fetal middle cerebral to uterine artery pulsatility index ratios in normal and pre-eclamptic pregnancies. Ultrasound Obstet Gynecol. 2006;28(6):794-801.
10. Pourcelot L. Clinical application of transcutaneous Doppler [in French]. Perroneau P, editor. Doppler ultrasound velocimetry 34 [in French]. Paris: INSERM; 1974. p. 213-40.
11. Salvesen DR, Higueras MT, Mansur CA, Freeman Brudenell JM, Nicolaides KH. Placental and fetal Doppler velocimetry in pregnancies complicated by maternal diabetes mellitus. Am J Obstet Gynecol.1993; 168: 645–652.
12. Landon MB, Gabbe SG, Bruner JP, Ludmir J. Doppler umbilical artery velocimetry in pregnancy complicated by insulin-dependent diabetes existing diabetes. Obstet Gynecol. 1989;73(6):961-5.
13. McCowan LM, Mullen BM, Ritchie K. Umbilical artery flow velocity waveforms and the placental vascular bed. Am J Obstet Gynecol 1987; 157: 900–902.
14. Jones CJ, Fox H. Placental changes in gestational diabetes. Obstet Gynecol 1976; 48: 274–280.
15. Saldeen P, Olofsson P, Parhar RS, al-Sedairy S. Prostanoid production in umbilical vessels and its relation to glucose tolerance and umbilical artery flow resistance. Eur J Obstet Gynecol Reprod Biol. 1996;68(1-2):35-41.
16. Giles WB, Trudinger BJ, Baird PJ. Fetal umbilical artery flow velocity waveforms and placental resistance: Pathological correlation. Br J Obstet Gynaecol 1985; 92: 31–38.
17. Alfirevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. Cochrane Database Syst Rev. 2010;(1):CD007529.
18. Tan AE, Norizah WM, Rahman HA, Aziz BA, Cheah FC. Umbilical artery resistance index in diabetic pregnancies: the associations with fetal outcome and neonatal septal hypertrophic cardiomyopathy. J Obstet Gynaecol Res. 2005;31(4):296-301.
19. Yalti S, Oral O, Gürbüz B, Özden S, Atar F.Ratio of middle cerebral to umbilical artery blood velocity in preeclamptic & hypertensive women in the prediction of poor perinatal outcome. Indian J Med Res 2004;120(1):44-50.
20. Jensen A, Roman C, Rudolph AM. Effects of reducing uterine blood flow on fetal blood flow distribution and oxygen delivery. J Dev Physiol 1991; 15: 309–323.
21. Dubiel M, Gudmundsson S, Gunnarsson G, Marsal K. Middle cerebral artery velocimetry as a predictor of hypoxemia in fetuses with increased resistance to blood flow in the umbilical artery. Early Hum Dev 1997; 47: 177–184.
22. Arias F. Accuracy of the middle-cerebral-to-umbilical-artery resistance index ratio in the velocimetry in pregnancies complicated by maternal diabetes mellitus. Am J Obstet Gynecol. 1993; 168(2):645-52.
23. Sterne G, Shields LE, Dubinsky TJ. Abnormal fetal cerebral and umbilical Doppler measurements in fetuses with intrauterine growth restriction predicts the severity of perinatal morbidity. J Clin Ultrasound 2001; 29: 146-51.
24. Graves CR. Antepartum fetal surveillance and timing of delivery in the pregnancy complicated by diabetes mellitus. Clin Obstet Gynecol. 2007;50(4):1007-13.
25. Björk O, Persson B. Villous structure in different parts of the cotyledon in placentas of insulin-dependent diabetic women. A morphometric study. Acta Obstet Gynecol Scand. 1984;63(1):37-43.
26. Shelly JH, Bassett JM, Milner RD. Control of carbohydrate metabolism in the fetus and newborn. Br Med Bull. 1975;31:37.

9/12/2013