Doppler Ultrasound Assessment of Fetal MCA and Umbilical Arteries in Patients with Gestational Diabetes versus Normal Pregnancies

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ABSTRACT

Background: It is unquestioned that gestational diabetes has a significant impact on pregnancy outcome. The embryo and the mother commonly experience serious complications directly attributable to diabetes.

Patients and Methods: A case control study was conducted in the department of Radiology Ain-shams university Hospital and some private centers to assess the impact of gestational DM on fetal middle cerebral and umbilical arteries Doppler indices to predict the possibility of adverse neonatal outcome. Seventy two patients were recruited for our study. They were divided into two groups. Control group (group 1) included 36 healthy pregnant women. Study group (group 2) included 36 gestational diabetic pregnant patients.

Results: Showed that gestational diabetic pregnancies are associated with an increased risk of fetal and neonatal risks compared with pregnancies in the healthy gravida as well as significant increase in MCA PI in gestational diabetic pregnancies with positive correlation to the neonatal complications.

Conclusion: MCA PI doppler in gestational diabetic mothers is important in the assessment of fetal well-being, and the follow up of pregnancy which helps in prevention of complicated delivery and adverse neonatal outcome.

Keywords: MCA; NICU; AEDF; REDF

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most frequently recorded morbidities of pregnancy. The incidence of GDM has risen over the past 30 years, mainly owing to a global increase in the prevalence of overweight and obesity and an increased pregnancy rate among women aged older than 35 years *(Scott-Pillai et al., 2013).*

The physiopathologic process underpinning the fetal adverse outcomes of maternal GDM is not fully understood but seems to be multifactorial. According to the Hyperglycemia and Adverse Pregnancy Outcomes study, the presence of maternal hyperglycemia is strongly associated with macrosomia and fetal hyperinsulinemia. Furthermore, elective cesarean delivery, neonatal hypoglycemia, premature delivery, birth injury, pre-eclampsia, admission to the neonatal intensive care unit, and hyperbilirubinemia are associated with the presence of GDM *(Dantas et al., 2019).*

Previous studies showed that materno–placental blood flow might change due to hyperglycemia during the pregnancy. As a consequence, redistribution of blood flow occurs from the peripheral vessels to the brain as a compensatory mechanism to the changes in placental hemodynamics *(Simanaviciute et al., 2006).*

This can be well traced by the Doppler ultrasound measurements of the umbilical (UA) and middle cerebral arteries (MCA) of the fetus *(Dorsey et al., 2018).*

Recently the assessment of the fetal cerebral blood flow velocities has become a suggested method in high-risk pregnancies *(Zanjani et al., 2014).*

AIM OF THE WORK

The aim of this work was to assess the fetal cerebral hemodynamic changes in diabetic pregnancies in comparison to normal pregnancies and its association with placental hemodynamic changes & pregnancy outcome (MCA & umbilical artery duplex).

PATIENTS AND METHODS

Type of Study: Case control study.

Study Setting: Radiology department-Ain shams university & some Private radiology centres.

Study Period: Two years.

Study Design: patients are referred for routine 3rd trimester ultrasound and diagnosed with gestational DM, Doppler ultrasound of the umbilical artery and MCA will be done on two groups of pregnant females (normal pregnancies and those with gestational DM) and data will be compared at the same gestational age.

Study Population: 72 pregnant females (36 with diabetes- 36 medically free).

Selection criteria for cases:

Inclusion Criteria: Pregnant females with gestational diabetes at 3rd trimester (28-40 w). Single baby. Any age.

Exclusion Criteria: Eclampsia & preeclampsia. Known cases of auto immune diseases, renal disease, blood disease, or hyperlipidemia. Pregnancy with maternal anemia or history of previous fetal anemia. Pregnant females with history of previous maternal or fetal complications of pregnancy. Other causes of high risk pregnancies with fetal IUGR.

Selection criteria for control

Inclusion Criteria: Pregnant females free from gestational diabetes at 3rd trimester (28-40 w). Single baby. Any age.

Exclusion Criteria: Gestational diabetes mellitus. Eclampsia & preeclampsia. Known cases of auto immune diseases, renal disease, blood disease, or hyperlipidemia. Pregnancy with maternal anemia or history of previous fetal anemia. Pregnant females with history of previous maternal or fetal complications of pregnancy. Other causes of high risk pregnancies with fetal IUGR.

Sample Size: Using G-power program, setting alpha error at 5% and power at 80% result from previous research *(Zanjani et al., 2014)* showed that the PI in middle cerebral artery in GDM +ve was 2.07+/- 0.4 compared to1.8+/- 0.4 in GDM -ve, based on this the needed sample is 36 +ve GDM & 36 -ve GDM females.

Ethical Considerations: Obtained a signed consent after reading the informed consent & explained the procedure details to the patients. The scientific ethical committee instructions are respected. The study groups inmcluded are not exposed to any harm or risk. Ensured confidentiality.

Study Tools

Procedure:

1. Full medical & blood sugar level history.

2. History of diabetis mellitus: RBS & HBA1C results are obtained from the patients laboratory records.

3. Routine pregnancy ultrasound: Biparietal diameter (BPD), Head circumference (HC), Femur length (FL), Abdominal circumference (AC) and Estimated fetal weight (EFW).

4. Umbilical artery & middle cerebral artery duplex.

Parameters used include:

- Umbilical artery & Fetal MCA pulsatility index (PI) & resistive index (RI).

- Umbilical artery and Fetal MCA peak systolic velocity (PSV): the highest velocity should be recorded.

- Umbilical artery & Fetal MCA systolic/diastolic (S/D) ratio: a normal fetal MCA S/D ratio should always be higher than the umbilical arterial S/D ratio.

- Cerebroplacental ratio (CPR): ratio of pulsatility index of MCA and umbilical artery.

RESULTS & DISCUSSION

The current study is a case control study that included seventy two patients (36 healthy pregnant women and 36 gestational diabetic pregnant women) recruited form Ain shams university clinics & some private scan radiology centers. It aimed to assess the fetal cerebral hemodynamic changes in diabetic pregnancies in comparison to normal pregnancies and its association with placental hemodynamic changes **&** pregnancy outcome.

Table (1): Fetal biometry in control versus patients group:

		Control group	Patients group	Test value	P-value	Sig.
		No. = 36	No. = 36			
Age	Mean ± SD	27.17 ± 5.85	31.11 ± 6.50	-2.706•	0.009	HS
	Range	20 – 42	19 – 42			
GA (weeks)	Mean±SD	31.58 ± 3.74	32.18 ± 3.62	-0.692	0.491	NS
	Range	27 – 38.4	26.71 – 38.43			
BPD	Mean±SD	72.63 ± 14.74	79.43 ± 9.70	-2.311	0.024	S
	Range	39.5 – 90.7	60.2 – 95			
HC	Mean±SD	236.47 ± 69.27	284.22 ± 38.89	-3.606	0.001	HS
	Range	143 – 331.3	205.2 – 390.3			
AC	Mean±SD	252.49 ± 62.32	276.77 ± 48.84	-1.840	0.070	NS
	Range	130 – 344	188.1 – 351			
FL	Mean±SD	54.85 ± 13.61	59.93 ± 9.65	-1.827	0.072	NS
	Range	26 – 73.5	43.2 – 75.5			
Fetal weight (g)	Mean±SD	1675.50 ± 888.81	1895.50 ± 789.01	-1.111	0.271	NS
	Range	400 – 2936	750 – 3440			
AFI (cm)	Mean ± SD	10.86 ± 1.66	15.93 ± 10.16	-2.936•	0.005	HS
	Range	7.5 – 15	5 – 36.5			
Fetal sex	Females	21 (58.3%)	19 (52.8%)	0.225*	0.635	NS
	Males	15 (41.7%)	17 (47.2%)			
FHR (bpm)	Mean ± SD	138.03 ± 10.67	149.61 ± 11.37	-4.457•	0.000	HS
	Range	120 – 182	124 – 189			
RBS (mg/dl) #	Mean ± SD	107.33 ± 16.84	166.75 ± 46.24	-7.245•	0.000	HS
	Range	80 – 137	90 – 250			
HBA1C #	Mean ± SD	4.65 ± 0.51	6.64 ± 0.88	-11.715•	0.000	HS
	Range	4 – 5.6	4.5 – 8.5			

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

*: Chi-square test; •: Independent t-test

#:Obtained from the latest patients laboratory records.

As shown in table (1), the participants were significantly older in the study group than in the control group (31.11 vs. 27.17 years, P = 0.009). There is statistically significant difference as regard BPD which is higher in gestational diabetic mothers (79.43ml) than the control group (72.63ml) P = 0.024, the HC of fetuses of gestational diabetic mothers is significantly higher than the control group (284.22 in patient group versus 236.47 in control group, P =0.001). A highly significant difference as regard AFI (15.93 in study group vs 10.86 in control group, P = 0.005), as well as fetal heart rate which is found significantly higher is study group as compared to the control group (149.61 in patients vs 138.03 in control, P = 0.000).

There is highly significant statistical difference between patient and control groups regarding RBS (166.75 in patient group versus 107.33 in control group, P = 0.000) as well as HBA1C (6.64 in patient group versus 4.65 in control group,   P=   0.000).

Table (2): Doppler parameters in control versus patients group:

		Control group	Patients group	Test value	P-value	Sig.
		No. = 36	No. = 36			
Umblical PI	Mean ± SD	1.03 ± 0.20	1.04 ± 0.18	-0.262•	0.794	NS
	Range	0.58 – 1.4	0.6 – 1.37			
Umblical RI	Mean ± SD	0.64 ± 0.07	0.62 ± 0.08	0.921•	0.360	NS
	Range	0.44 – 0.8	0.4 – 0.73			
MCA PI	Mean ± SD	1.69 ± 0.36	1.90 ± 0.36	-2.462•	0.016	S
	Range	1.03 – 2.9	1.03 – 2.7			
MCA RI	Mean ± SD	0.76 ± 0.05	0.77 ± 0.09	-0.485•	0.629	NS
	Range	0.7 – 0.9	0.53 – 0.92			
MCA PSV (cm/s)	Mean ± SD	41.96 ± 8.02	42.10 ± 11.75	-0.058•	0.954	NS
	Range	30.33 – 60.47	21.44 – 67.04			
Cerebro- placental ration (mcaPI/umPI)	Mean ± SD	1.70 ± 0.51	1.88 ± 0.49	-1.558•	0.124	NS
	Range	0.8 – 3	1 – 3			
MCA ED	Mean ± SD	9.09 ± 2.60	9.43 ± 3.68	-0.453•	0.652	NS
	Range	3.2 – 16.6	1.9 – 18			
MCA S/D ratio	Mean ± SD	4.95 ± 1.72	5.18 ± 3.55	-0.352•	0.726	NS
	Range	2.97 – 10.69	2.73 – 23.94			
UA PSV	Mean ± SD	44.80 ± 7.48	43.07 ± 10.52	0.805•	0.424	NS
	Range	30.74 – 61.96	24.93 – 79.33			
UA ED	Mean ± SD	15.51 ± 3.63	16.06 ± 6.01	-0.470•	0.640	NS
	Range	7.78 – 23.27	5.45 – 29.63			
UA S/D ratio	Mean ± SD	2.99 ± 0.66	2.86 ± 0.62	0.860•	0.393	NS
	Range	1.79 – 4.89	1.81 – 4.71			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
•: Independent t-test

As shown in table (2), there is statistically significant difference regarding the mean MCA PI between patient and control group which is higher in patient (1.69) versus (1.90) in control group with P= 0.016 .

There is no statistically significant difference between the mean of the rest of MCA and UA studied parameters with P value above 0.05.

The aforementioned significantly different values between case and control groups (BPD, HC, AFI, FHR, RBS, HBAIC, neonatal complications and maternal complications) will be correlated with the patients Doppler parameters of UA & MCA in the following tables:

Table (3): Maternal & fetal outcome in control versus patients group:

		Control group	Patients group	Test value	P-value	Sig.
		No. = 36	No. = 36			
Neonatal complications	No	29 (80.6%)	21 (58.3%)	4.189*	0.041	S
	Yes	7 (19.4%)	15 (41.7%)			
Maternal complications	No	33 (91.7%)	26 (72.2%)	4.600*	0.032	S
	Yes	3 (8.3%)	10 (27.8%)			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test

There is significant difference regarding neonatal complications as well as maternal complications which are found to be higher is patient group than in control group. 15 pregnant female with gestational diabetes had neonatal complication compared to 7 in control group (P value= 0.041).

		Neonatal complications		Test value	P-value	Sig.
		No	Yes			
		No. = 21	No. = 15			
Umblical PI	Mean ± SD	1.03 ± 0.21	1.06 ± 0.13	-0.368•	0.715	NS
	Range	0.6 – 1.36	0.9 – 1.37			

Umblical RI	Mean ± SD	0.63 ± 0.09	0.62 ± 0.07	0.276•	0.785	NS
	Range	0.4 – 0.73	0.5 – 0.7			
MCA PI	Mean ± SD	1.77 ± 0.3	2.07 ± 0.37	-2.704•	0.011	**S**
	Range	1.03 – 2.2	1.6 – 2.7			
MCA RI	Mean ± SD	0.75 ± 0.09	0.8 ± 0.07	-1.734•	0.092	NS
	Range	0.53 – 0.92	0.67 – 0.9			
MCA PSV (cm/s)	Mean ± SD	40.5 ± 11.08	44.33 ± 12.66	-0.965•	0.342	NS
	Range	21.44 – 67.04	23.5 – 60			
Cerebro- placental ration (mcaPI/umPI)	Mean ± SD	1.84 ± 0.47	1.94 ± 0.52	-0.569•	0.573	NS
	Range	1 – 3	1.32 – 3			
MCA ED	Mean ± SD	10 ± 3.7	8.7 ± 3.6	1.031•	0.310	NS
	Range	4.9 – 17.6	1.9 – 18			
MCA S/D ratio	Mean ± SD	4.36 ± 1.29	6.34 ± 5.16	-1.698•	0.099	NS
	Range	2.79 – 7.81	2.73 – 23.94			
UA PSV	Mean ± SD	41.47 ± 10.56	45.31 ± 10.41	-1.082•	0.287	NS
	Range	24.93 – 60.5	37.91 – 79.33			
UA ED	Mean ± SD	15.51 ± 6.86	16.84 ± 4.68	-0.651•	0.519	NS
	Range	5.45 – 29.63	10.78 – 29.6			
UA S/D ratio	Mean ± SD	2.93 ± 0.7	2.76 ± 0.48	0.802•	0.428	NS
	Range	1.81 – 4.71	2 – 3.65			

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

•: Independent t-test

- There is positive correlation as regard neonatal correlation and MCA PI in patient group with P value =0.011.

- No significant correlation between neonatal complication and the rest of studied doppler parameters.

- Our results demonstrated that gestational diabetic pregnancies are associated with an increased risk of fetal and neonatal risks compared with pregnancies in the healthy women.15 pregnant female with gestational diabetes had neonatal complication compared to 7 in control group (fetal macrosomia, respiratory distress, NICU admission, low birth weight, cyanosis, cardiac abnormalities, hydrocephalus, renal agenesis, pneumonia, IUFD and neonatal death) (P= 0.041).In addition, there was no statistically significant differences in umbilical artery, middle cerebral artery Doppler indices and cerebroplacental ratio between the two groups apart from MCA PI which is found to be significantly higher is gestational diabetic pregnancies compared to healthy group. (Mean in control group= 1.69 ± 0.36 Mean in patient group= 1.90 ± 0.36 with P value = 0.016).

- Furthermore, the frequency of neonatal complications was positively correlated with MCA PI in pregnancies complicated with gestational DM (P value =0.011).

- The present results are in line with the results reported in a study by *Zanjani et al.* Shabani Zanjani and his colleagues study 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 two groups of study; except for the left fetal MCA-PI, which was significantly higher in GDM group. They concluded that gestational diabetes may contribute to an elevated PI in the fetal MCA *(Zanjani et al., 2014).*

- On the other hand *Leung et al.,* found that UA-PI, MCA-PI and MCA-Vmax was not useful in the prediction of abnormal pregnancy outcome in GDM. A prospective study was performed on 169 singleton GDM pregnancies. Doppler parameters of UA as well as MCA were measured every 4 weeks until delivery from the time of diagnosis of GDM. The pregnancy outcome was obtained from the hospital database *(Leung et al., 2004).*

- A similar result was achieved by *Salvesen et al.,* placental and fetal circulation were investigated in pregnancies complicated by maternal diabetes mellitus and were related to the changes to fetal blood pH, P_{O2}, and hematocrit. Their study included 65 well-controlled diabetic pregnancies in a cross-sectional study. In 41 cases cordocentesis was also performed for the measurement of umbilical venous blood pH, P_{O2}, and hematocrit. And they concluded that maternal diabetes mellitus is not associated with abnormalities in Doppler indexes of the placental or fetal circulations *(Salvesen et al., 1993).*

- **The advantage of our study** is that we correlated the archived Doppler parameters of MCA and UA with the fetal biometry and the pregnancy (maternal and fetal) outcome, however some of the collected data of the effect of gestational diabetes on fetus were not in line with the diabetic complications this may refer to associated subclinical maternal infections, the dependence on the mother in history taking not on medical files, corona virus pandemic and its effect on blood flow, blood vessels and coagulation process.
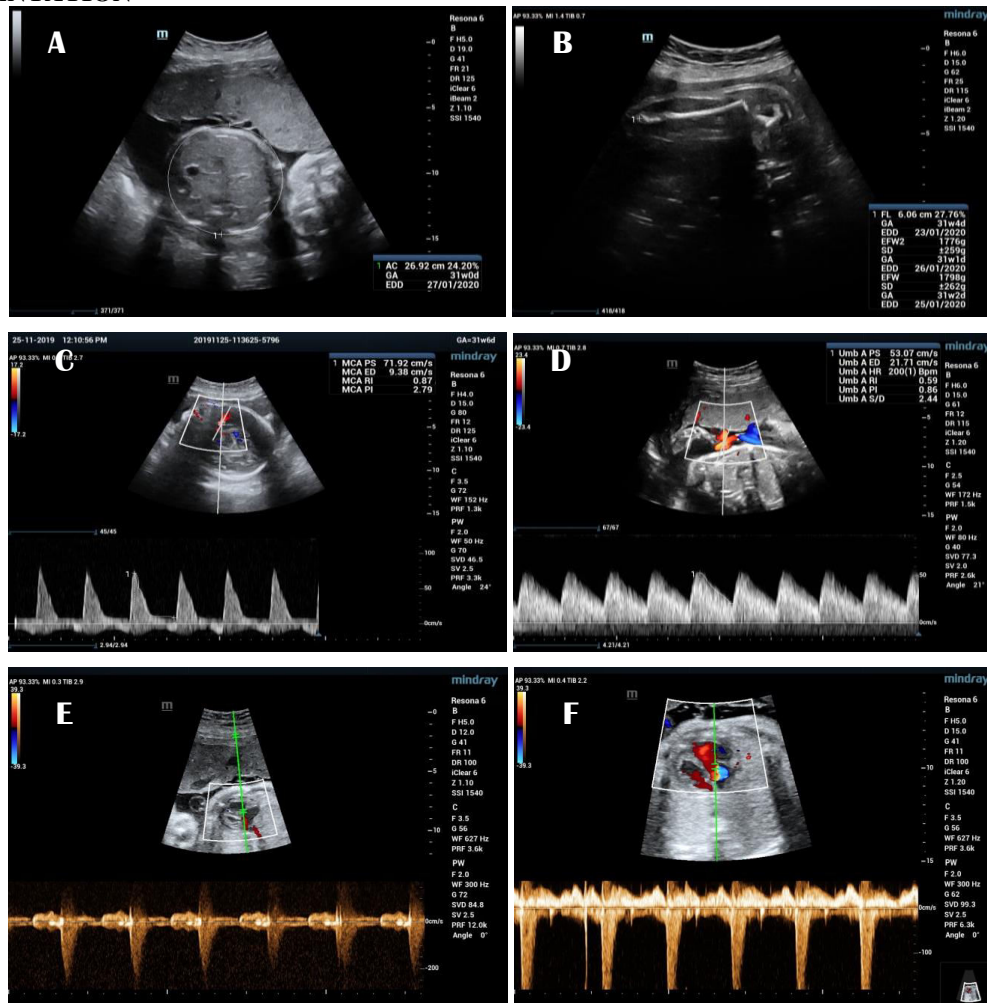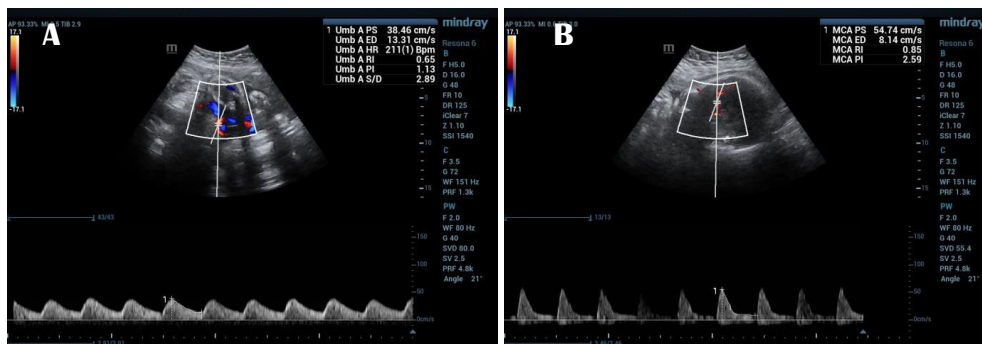
CASE PRESENTATION

Figure (1): 37 year-old pregnant female (GA 31+6) diagnosed GDM with no history of any medical disorders, came to our hospital for routine obstetric examination RBS=190 HBA1C= 6.5, MCA PI =2.7, MCA PSV=58.34 cm/sec, tricuspid regurge by ultrasound, outcome: vaginal delivery at 38+6 GA, 10 day-NICU admission. No maternal complications. **(A&B)** show gestational age 31+6 weeks gestation, **(C&D)** show Doppler waveforms of MCA and UA. **(E&F)** show ultrasound evidence of tricuspid regurgitation (reversed flow more than 80 cm/sec and its interval extends to more than half of systole)
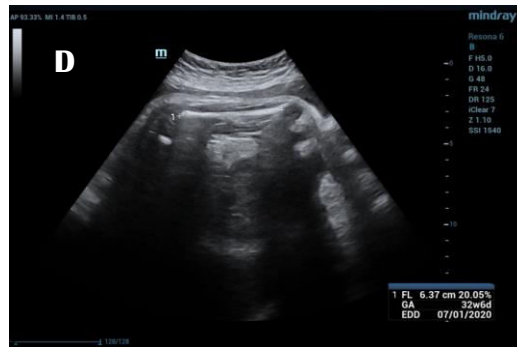
Figure (2): 32 year-old pregnant female (GA 33+5 by scan, 30+2 by LMP) diagnosed GDM with no history of any medical disorders, came to our hospital for routine obstetric examination RBS=145, HBA1C= 7, MCA PI =2.5, MCA PSV=54.74 cm/sec, mild fetal macrosomia by ultrasound fetal weight by ultrasound =2510 Kg, outcome: cesarean section at 38 weeks GA, macrosomic baby with birth weight 4.3 Kg 1 day-NICU admission to stabilize respiration. No maternal complications.**(A&B)** show Doppler waveforms of MCA and UA, **(C)** shows femur length with corresponding gestational age 32+6 days.
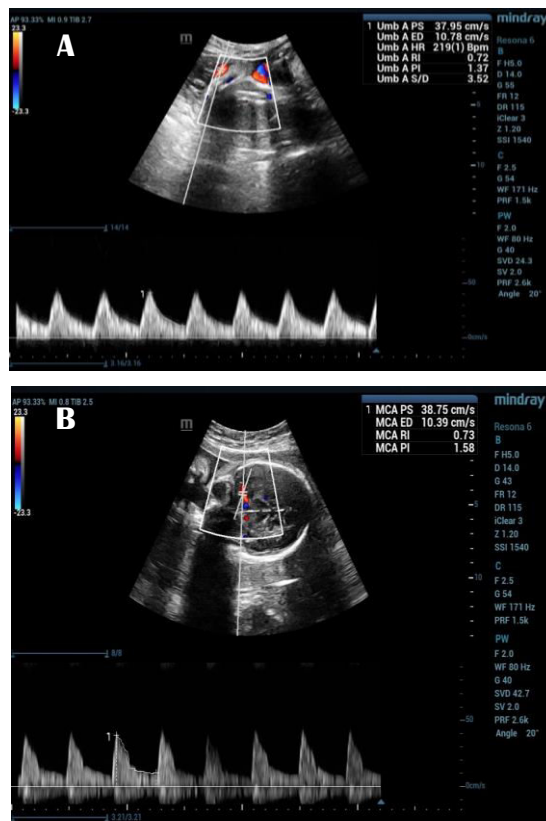

Figure (3): 31 year-old pregnant female (GA 31+2) diagnosed GDM with no history of any medical disorders, came to our hospital for routine obstetric examination RBS=233, HBA1C= 8, MCA PI =1.5, MCA PSV=38.75 cm/sec, Slightly echogenic bowel by ultrasound, outcome: cesarean section at 32 + 5 GA, 28 day-NICU admission followed by neonatal death from necrotizing enterocolitis. No maternal complications.**(A&B)** show Doppler waveforms of MCA and UA at 31 + 2 GA fetus.

CONCLUSION

From our study, we can conclude that antenatal fetal cerebral doppler ultrasound surveillance is an essential component of the standards of care in management of pregnancies complicated with gestational diabetes.

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