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The value of Middle cerebral and umbilical arteries Doppler indices in pregestational diabetic versus normal pregnancies in prediction of adverse neonatal outcome

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Synopsis
Maternal DM is not associated with significant Doppler abnormalities. UA and MCA had low sensitivity in the prediction of adverse neonatal outcome

Impact statement
What is already known on this subject?
Doppler velocimetry was introduced as an important fetal well-being test.

the results of Doppler studies in pregnancies complicated by diabetes are conflicting

- What do the results of this study add?

The sensitivity and specificity of umbilical artery Doppler in the prediction of adverse neonatal outcomes among diabetic patients were 25% and 88.89%, respectively, while, the sensitivity and specificity of middle cerebral artery Doppler were 20.83% and 91.67%, respectively.

- What are the implications of these findings for clinical practice and/or further research?

Maternal DM is not associated with significant abnormalities in Doppler indices of placental or fetal circulation.

Both UA and MCA had low sensitivity in the prediction of adverse neonatal outcome. These cannot be used as a single evaluation test for fetal well being.

Abstract

Objectives: To study the impact of pregestational DM on fetal middle cerebral (MCA) and umbilical arteries (UA) Doppler indices and hence, evaluating their diagnostic

performance as predictors for adverse neonatal outcome.

Methods: The study included 2 equal groups of 60 patients each, thus making up a total of 120 patients; control group of healthy pregnant women and study group included pregnant patients known to have pregestational diabetes. The study group was furtherly subdivided into two equal subgroups of 30 patients each. This sub classification was made according to to HbA1C levels namely; controlled diabetics (defined as those having HbA1C < 6.5 %) and uncontrolled diabetics (defined as those having values of HbA1C ≥ 6.5 %). UA, MCA Doppler indices (resistance index and pulsatility index) and Cerebroplacental Doppler ratio were measured for each patient. Neonatal outcome was assessed and recorded following delivery. The following parameters were assessed: neonatal blood sugar, 1min and 5min Apgar score and admission to neonatal intensive care unit.

Results: The sensitivity and specificity of umbilical artery Doppler in the prediction of adverse neonatal outcomes among diabetic patients were 25% and 88.89%, respectively, while, the sensitivity and specificity of middle cerebral artery Doppler were 20.83% and 91.67%, respectively. The resistance index and pulsatility index of MCA and UA were not of significant corelation with any of the neonatal outcomes (Pearson's r ranged -0.07 to 0.13, $p > 0.05$).

Conclusion: maternal DM is not associated with significant abnormalities in Doppler indices of placental or fetal circulation. In addition, both UA and MCA had low sensitivity in the prediction of adverse neonatal outcome.

Keywords: Diabetes mellitus, Umbilical artery, Middle cerebral artery Doppler ultrasound and adverse neonatal outcome.

Introduction

The prevalence of Diabetes mellitus (DM) in the pregnant population in the United States is stated to be 6-7%. It is classified into pre-gestational DM (PGDM) and gestational DM (GDM) (1).

Pregestational DM poses an increased risk for the mother, the fetus and the neonate (2). Congenital malformation (e.g., cardiac or Musculo-skeletal) occurs more frequently in pregestational diabetic women and approximately 50% of such women deliver macrosomia babies with consequent risk of birth related trauma, and the development of type 2 diabetes mellitus, metabolic syndrome, vascular and cardiac diseases later in life (3 & 4). On the other hand, long standing preexisting DM before current pregnancy poses a higher risk of vasculopathy involving the uterine arteries thus resulting in abnormal development of the uteroplacental circulation and consequently placental insufficiency & restricted fetal growth (5). Those with suboptimal glycemic control have higher risk of developing such complications (6).

The pregnancy outcome in this pregnant population could be improved by approaching different targets. Health education should be delivered to all patients ensuring following adequate balanced diet, adhering to drug treatment, and the role of optimum glycemic control on pregnancy outcome (7).

Fetal surveillance in high-risk pregnancies has been a matter of concern, with the aim of achieving optimum pregnancy outcomes in such group of However, till the present date, no method of fetal surveillance was proved to be superior (8). Doppler velocimetry was introduced as an important fetal well-being test. It measures the blood flow through arteries and veins, such as umbilical and middle cerebral arteries. However, the results obtained regarding the use of Doppler studies

in pregnancies complicated by diabetes were conflicting. In fact, despite their widespread application, few studies have investigated their role as effective tools in ameliorating perinatal outcomes among such population of pregnant mothers. (1).

Shabani Zanjani and his colleagues (9) studied the Doppler indices of fetal brain hemodynamics among pregnant women with GDM compared to healthy ones and reported that the pulsatility index (PI) of the middle cerebral artery (MCA) was Increased among diabetic group compared to the healthy group. On the other hand, Niromanesh and his colleagues (10) compared the umbilical artery (UA) and MCA Doppler indices as fetal well-being tests in diabetic pregnant women (whether gestational or pregestational) and they claimed that UA Doppler indices were better than MCA indices in the prediction of adverse neonatal outcomes but both had low sensitivity.

Hence, we performed this study to evaluate of effect pregestational diabetes on fetal middle cerebral and umbilical arteries Doppler indices and to evaluate their validity as predictors of poor neonatal outcome in pregnancies complicated by diabetes.

Methodology

The current study is a Cross-sectional one conducted in the Obstetrics & Gynecology department (Kasr El-Aini Hospital – Faculty of Medicine - Cairo University) in the time period from July 2019 to October 2020. One hundred and twenty pregnant women (aged from eighteen to forty years old) with living health singleton fetus between 34-37 weeks gestation (confirmed by either the 1st day of the LMP or 1st trimesteric ultrasound scan) were recruited and they were divided into two equal groups of 60 each; Control group that included healthy pregnant women and Study group that included pregestational diabetic pregnant patients. The latter group was furtherly subdivided into two subgroups according to HbA1C levels namely; controlled diabetics (included 30 diabetic pregnant women with controlled DM defined as HbA1C less than 6.5%) and uncontrolled diabetics (included 30 diabetic pregnant women with uncontrolled DM defined as HbA1C equal to, or more than 6.5%). The study was approved by the Hospital Ethical Committee & was registered at ClinicalTrial.gov registry (The registry number: NCT03915990).

Diabetic women with either complicated diabetes or any other concomitant chronic disorder (e.g., hypertension or renal disease) were excluded. Patients with growth-restricted (EFW less than the 10th percentile for the corresponding gestational age) or malformed fetuses were excluded. Patients with any superimposed medical disorders, oligohydramnios (AFI below the fifth percentile) or rupture of membranes in the current pregnancy were also omitted.

Informed consent was obtained from all participants (after explaining the aim of the study and discussing the potential hazards) then all candidates who met the eligibility criteria were subjected to the following: full history taking, thorough physical examination (including maternal body weight and the 1st day of the LMP) followed by obstetric ultrasound to confirm the eligibility of the current pregnancy to participate in the study (by confirming gestational age & excluding fetal anomalies or oligohydramnios) and to assess the fetal weight and amniotic fluid index (to detect presence of macrosomia and polyhydramnios (defined as EFW above 90th percentile for gestational age and AFI more than 95th percentile, respectively). Laboratory investigations (complete blood picture, fasting and post prandial blood sugar, liver & kidney functions and HbA1C estimation) were also done.

Doppler ultrasonography assessment was done using Samsung SonoAce R3 abdominal probe convex linear transducer 3.5 MHZ equipped with color and pulsed Doppler

capabilities (SonoAce R3, SAMSUNG MEDISON CO., Gangnam-gu, Seoul, Korea). As regard umbilical artery (UA) Doppler, participants were examined in a semi-recumbent position with a left lateral tilt. The uterine content was scanned and an area of amniotic cavity with many free loops of cord was selected. The characteristic sound and shape of the umbilical artery were identified using a pulsed wave Doppler applied on a free loop of cord. The image was frozen when at least 3 consecutive waves of similar height appeared on the screen and umbilical artery Resistance index (RI) and pulsatility index (PI) were calculated. The final values were obtained after a minimum of 3 separate readings were averaged. Umbilical artery Doppler evaluations were performed during fetal apnea (to nullify effect of fetal breathing movements on waveform variability) and avoided during fetal activity (11). Abnormal UA Doppler velocimetry was considered when UA indices exceeded the 95th centile for the corresponding gestation or when the diastolic flow was either reversed or absent (figure 1&2).

As for the evaluation of the middle cerebral artery (MCA) Doppler indices, the fetal brain was scanned at the level of the biparietal diameter and a transverse view was obtained then the probe was advanced towards the base of the skull till the level of the lesser wing of the sphenoid bone. The middle cerebral artery was identified using color flow imaging being the major lateral branch of the circle of Willis that runs anterolaterally at the margin between the anterior and the middle cerebral fossae. The flow velocity waveforms were obtained by placing the pulsed Doppler sample gate on the middle portion of the artery. The image was frozen when at least 3 consecutive waves of similar height appeared on the screen and MCA RI &PI were calculated. The final values were obtained after a minimum of 3 separate readings were averaged. As fetal head compression may alter intracranial arterial waveforms, subsequently, no or minimal pressure should be applied to maternal abdomen during the scan (12). Abnormal MCA Doppler velocimetry was considered when MCA indices were below the 5th centile for the corresponding gestational age (figure 3&4). All ultrasounds and Doppler evaluations were done by the same sonographer (Rasha El-komy).

The following data were recorded; gestational age at Doppler study and termination, presence of macrosomia or polyhydramnios, Doppler indices for UA & MCA, mode of delivery and neonatal outcomes (i.e., birth weight, 1- & 5-minutes Apgar score, blood sugar at birth, admission to neonatal intensive care unit). Abnormal perinatal outcomes were considered in the presence of any of the following four events: 1-& 5- minutes Apgar scores below 7, neonatal blood sugar less than 50 mg/dl (neonatal hypoglycemia) and neonatal intensive care unit (NICU) admission. Patients with at least one adverse neonatal event were categorized in the abnormal neonatal outcome group.

Primary outcome measured the difference in Doppler indices values (RI&PI) for umbilical and middle cerebral arteries between the control (non-diabetic) and the study group (diabetics whether controlled or uncontrolled). The sensitivity and specificity of umbilical artery and middle cerebral artery Doppler indices (RI&PI) as predictors for adverse neonatal outcomes among diabetic women were assessed as secondary outcomes.

The sample size was calculated according to the figures obtained from Shabani Zanjani and his colleagues (9) using the Pulsatility Index (PI) of the left MCA Doppler. The mean PI for MCA Doppler in the first group (gestational diabetic cases) was 2.07 and the second group (non-diabetic cases) was 1.85. The standard deviation (SD) used for calculation was 0.40. The ratio of enrollment for the study to control was 1:1. The power was set at 0.8 and Alpha error at 0.05. This

gave us the sample of 52 patients in each group, we raised the sample size by 15% to avoid dropouts thus giving us 60 cases in each study arm. Sample size was calculated using Sample Size Calculator ClinCalc.com last accessed on 2/4/2017.

Data were coded and entered using the statistical package SPSS version 25. Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups were done using unpaired t test in normally distributed quantitative variables, while non-parametric Mann-Whitney test was used for non-normally distributed quantitative variables (13). For comparing categorical data, Chi square (|2) test was performed. Exact test was used instead when the expected frequency was less than 5 (14). Correlations between quantitative variables were done using Spearman correlation coefficient (15). Logistic regression was done to detect independent predictors of cases (16). P-values less than 0.05 were considered as statistically significant.

Results

This prospective study included one hundred and twenty patients who met the inclusion criteria. Flow of patients was demonstrated in figure 5.

Study versus control group analysis

Patients' characteristics and laboratory parameters together with pregnancy characteristics and neonatal outcomes were summarized in table 1. Regarding adverse neonatal outcome, there was a statistically significant difference between the study and control group in 3 out 4 parameters defined in methodology namely; the frequency of neonatal hypoglycemia, 1-minute Apgar score at 1minute (below 7) and Apgar score at 5 minutes (below 7) (table 2).

Our results showed no statistically significant difference between the mean RI & PI of **umbilical artery** in the study group (RI= 0.63& PI=0.93) and the control group (RI = 0.61 & PI = 0.95; P value =0.057 &0.659, respectively). Similarly, there was no statistically significant difference between the mean RI &PI of the **middle cerebral artery** between the study group (RI = 0.8 & PI=1.73) and the control group (RI=0.83 & PI=1.81; P value =0.07 &0.322, respectively). Consequently, the difference between the mean **Cerebroplacental Doppler ratio** (MCA/UA PI) in both groups was not statistically significant (1.94 in the study group versus 1.92 in the control group; P=0.754) (table 3).

Controlled diabetics versus uncontrolled diabetics

Patients' characteristics and laboratory parameters together with pregnancy characteristics and neonatal outcomes were summarized in table 4. Regarding adverse neonatal outcome, there was no statistically significant difference between the controlled and uncontrolled group in all parameters defined in methodology (table 5).

There was no statistically significant difference between the mean RI &PI of **umbilical artery** in the controlled group (RI = 0.62 & PI = 0.92) and the uncontrolled group (RI = 0.64 & PI= 0.94; P value =0.5 & 0.764, respectively). Similarly, there was no statistically significant difference between the mean RI & PI of the **middle cerebral artery** between the controlled group (RI= 0.81 & PI = 1.77) and the uncontrolled group (RI = 0.79& PI = 1.69; P value =0.52& 0.488 respectively). Hence, the difference between the mean **Cerebroplacental Doppler ratio** (MCA/UA PI) in both groups was not statistically significant (1.98 in the controlled diabetic group versus 1.9 in the uncontrolled diabetic group; P value =0.46) (table 6).

Predictive value of umbilical artery & middle cerebral artery Doppler indices in the diabetic group

Adverse neonatal outcomes were detected in 24 neonates out of 60 among those included in the study group. Umbilical artery Doppler indices (abnormal RI & PI) correctly identified only six of them, while, middle cerebral artery Doppler indices correctly identified only five of them. Based on data, the sensitivity and specificity of umbilical artery and middle cerebral artery Doppler tests in the prediction of adverse neonatal outcomes were calculated and the results are summarized in table (7).

Logistic regression to detect independent predictors of cases

We performed a multivariate logistic regression to identify factors associated with cases compared to control group. We have found that only PPBS was more likely to be associated with the study group (odds ratio (OR): 1.32, 95% Confidence Interval: 1.05-1.66, p= 0.018) (table 8).

Correlation analysis of umbilical artery & middle cerebral artery Doppler indices with neonatal outcome

The RI and PI of umbilical artery in the study group were not significantly correlated with the Apgar score at 1 minute (Pearson's r = -0.07, p = 0.58), Apgar score at 5 minutes (r = -0.14, p = 0.28) or neonatal hypoglycemia (r = -0.12, p= 0.35). Similarly, the RI and PI of middle cerebral artery were not significantly correlated with Apgar score at 1 minute (r = -0.03, p = 0.80), Apgar score at 5 minutes (r = 0.07, p = 0.58) or neonatal hypoglycemia (r= 0.13, p = 0.34) (table 9).

Discussion

Diabetes is a multisystem chronic disease that requires vigilant medical care and implementation of different strategies for risk reduction beside optimum glycemic control. Patient support and health education form the cornerstone of management of those cases in order to prevent acute complications and reduce the risk of long-term complications. Several strategies have been developed in order to improve the outcome of diabetes. (17).

The care of women with pregestational diabetes should be delivered ideally by multidisciplinary team in a multidisciplinary setting that consists of an endocrinologist, maternal-fetal medicine specialist, dietitian and diabetes educator, when available (17).

Fetal surveillance is an important tool in the care of such pregnancies, complicated with PGDM or GDM. Doppler velocimetry is one of the most important methods of antenatal surveillance. In the present study, we examined whether UA and MCA Doppler measurements could help to sort out fetuses at risk of jeopardized outcomes in case of maternal DM.

Our results showed that fetal and neonatal risks were higher with pregnancies complicated by pregestational diabetes in comparison to their healthy counterparts. However, this difference was not shown to be present in the measurements of umbilical artery (UA), middle cerebral artery (MCA) and cerebroplacental ratio Doppler. Furthermore, neonatal outcome was jeopardized in uncontrolled diabetic group compared to controlled diabetic group, but this was not statistically significant. In addition, our results failed to demonstrate any difference of statistical significance in umbilical artery, middle cerebral artery Doppler indices and cerebroplacental ratio between the two subgroups of pregnant patients with pregestational diabetes. Both UA and MCA assessments had low sensitivity in the prediction of adverse neonatal outcome (25% and 20.83%, respectively) whereas their specificity were 89% and 92%, respectively.

Our results showed that maternal DM does not adversely affect Doppler indices. This finding was in harmony with the results reported in a study by Salvesen and his co-workers (18). They investigated the effect of maternal diabetes on both placental and

fetal circulation in relation to any changes in fetal blood pH, PO2, and hematocrit; but the study included only well-controlled diabetic pregnancies (65 cases). They concluded that there was no association between maternal DM abnormal Doppler indices of placental or fetal circulation.

Likewise, Ben-Ami and his colleagues (19) evaluated the role systolic to diastolic ratio (S/D ratio) of the umbilical artery in the prediction of perinatal outcome in diabetic pregnancies. Their study included 92 diabetic pregnant women of gestational age from 28 to 40. the sensitivity and specificity of the Doppler studies as a predictor of poor perinatal outcome had a sensitivity and specificity of 39% and 92%, respectively, thus failing to prove any association of maternal diabetes to S/D ratio abnormalities in fetuses who had an inferior outcome to their counterparts. They concluded that the S/D ratio of the umbilical artery was not superior to other surveillance tests in the management of diabetic pregnancies.

The current results showed that sensitivity of both UA and MCA Doppler tests was low for neonatal outcomes. These findings are not different than the results reported by Niromanesh and his colleagues (10). They compared MCA and UA Doppler indices for the evaluation of fetal well-being in 103 pregnant mothers with pre-gestational or gestational diabetes mellitus. Those who had abnormal UA or MCA Doppler test results were candidates for pregnancy termination either by labor induction or cesarean section, which was decided upon set criteria. The outcomes included one- and five-minute Apgar score, admission to NICU, metabolic disturbances as acidosis, hypoglycemia, hypocalcemia, in addition to gestational age at delivery, and neonatal death. 48 women had poor perinatal outcomes; 17.5% and 9.7% of women had abnormal UA and MCA Doppler test results, respectively. They concluded that though abnormal UA and MCA Doppler tests were associated with adverse neonatal outcomes; yet both tests had low sensitivity in the prediction of adverse neonatal outcomes (ranged between 20% and 60%).

In another study, Niromanesh and his colleagues (20) compared between the efficacy of the non-stress test (NST) to that of the umbilical artery (UA) Doppler assessments in the prediction of adverse perinatal outcomes in 50 pregnant women with GDM. Totally, 22% and 12% of women had an abnormal UA Doppler and a non-reactive NST respectively; 13 women had poor outcomes. Women with non-reactive NST ($p<0.001$) and abnormal UA Doppler ($p=0.033$) had a higher prevalence of poor neonatal outcome. The sensitivity and specificity of the NST in predicting different poor outcomes were 76.9% and 97.3% respectively, whereas that UA Doppler in predicting different poor outcomes were 30.8% and 94.6% respectively. Accordingly, they concluded that NST was far more superior to UA in the prediction of adverse perinatal outcomes in patients with GDM.

Moreover, Yalti and his colleagues (21) stated that Umbilical velocimetry, is an assessment tool for placental function only and is not a direct reflection of the fetal status. In their study, sensitivity, positive predictive values of umbilical artery Doppler indices alone were 30 and 50 per cent respectively.

To the contrary, Shabani Zanjani and his colleagues (9) studied the effects of GDM on Doppler parameters (fetal MCA and UA) in comparison to normal pregnancies. The study was performed on 66 pregnant women, including 33 women with GDM and 33 healthy pregnant patients. Peak systolic and diastolic velocities, PI, RI and systolic diastolic ratio (SD) were recorded in UA as well as both right and left fetal MCAs for every recruited pregnant woman by means of Doppler ultrasonography. The mean gestational age at the time of examination was 34.45 weeks in GDM group. Although, the study group had higher Doppler indices values compared to their healthy counterparts; yet this was not

statistically significant. However, only the left fetal MCA-PI, was significantly higher in GDM group; for which they concluded that gestational diabetes may contribute to an elevated PI in the fetal MCA. However, the small sample size with the consequent low statistical power and the lack of access to follow up data, were two major limiting factors to this study.

To the best of our knowledge, the current study is the first one that compared fetal middle cerebral and umbilical arteries Doppler indices in pregestational diabetic versus normal pregnancies. Most of the former studies focused more on the blood flow of umbilical artery and fetal vessels in patients with gestational DM (GDM). Furthermore, we evaluated any difference that could be impacted upon the Doppler indices by glycemic control. We also excluded patients with other concomitant medical disorders to avoid the effect of other confounding variables on Doppler indices.

The first shortcoming of this study was the small sample size that led to low statistical power in between the groups of comparison. Although the rate of poor neonatal outcomes in our sample was about 40%, the outcomes were not associated with abnormal Doppler test results of fetal circulation. This may be due to the outcomes were not severe enough to affect fetal circulation. Further studies and systematic reviews are warranted to reach a precise answer about the best surveillance test for fetal evaluation among diabetic mothers.

In conclusion, maternal DM is not associated with abnormal changes in Doppler indices of placental or fetal circulation (irrespective of the glycemic control). In addition, both UA and MCA assessments had low sensitivity in the prediction of adverse neonatal outcome.

- The authors declare no conflict of interest.
- Funding: self-funded.

Declarations

Ethics approval and consent to participate Kasr Alainy ethical committee approval.

Consent for publication all participants agave their consent for publication

Informed consent: Informed consent was obtained from all individual participants included in the study.

Availability of data and materials: not applicable

Competing interests, No conflict of interest

Funding Self fund

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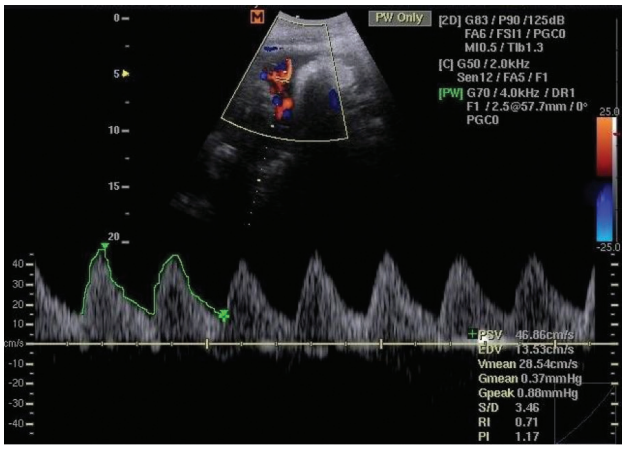

Figure (1): Umbilical artery Doppler for uncontrolled diabetic with adverse neonatal outcome (1-min APGAR score was less than 7).

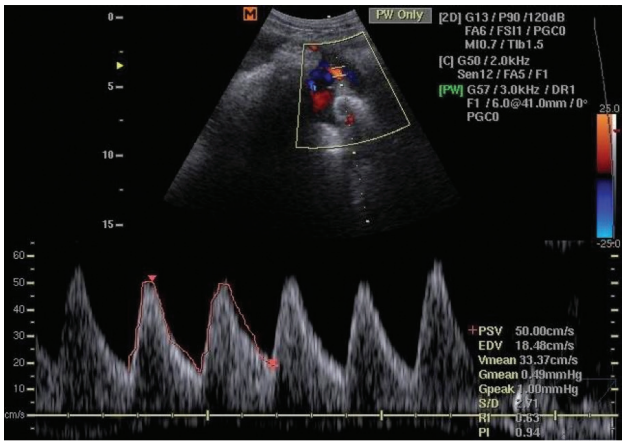

Figure (2): Umbilical artery Doppler for non-diabetic pregnant woman.

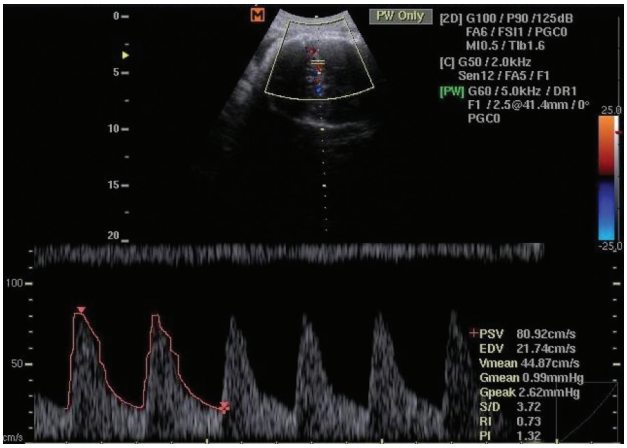

Figure (3): Middle cerebral artery Doppler for controlled diabetic women with adverse neonatal outcome (neonatal blood sugar 40mg/dl& 1-min APGAR score less than 7).

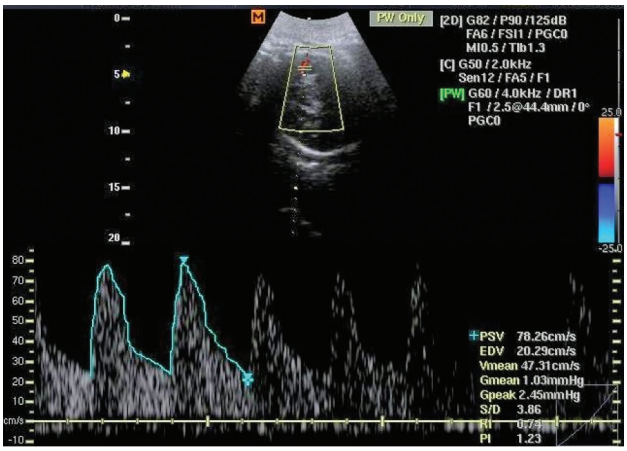

Figure (4): Middle cerebral artery Doppler for healthy pregnant women.

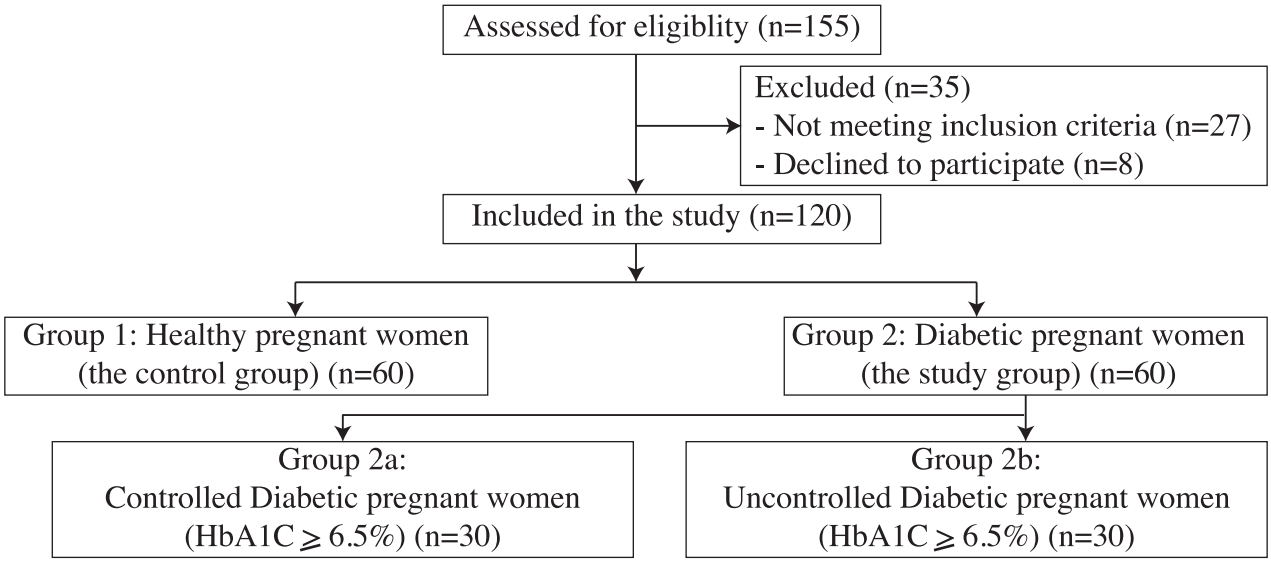

Figure (5): flow chart of the participants.

Table (1): Patients characteristics and laboratory parameters, pregnancy characteristics and neonatal outcome in the study and control groups.

Variable	Study group	Control Group	P value
Maternal Age (Y, Mean ± SD)	30.45 ± 5.80	27.77 ± 5.76	0.012
BMI (kg/m², Mean ± SD)	30.37 ± 4.468	30.8 ± 4.337	0.591
Primigravidas (No., %)	12 (20%)	18 (30%)	0.606
FBS (mg/dl, mean ± SD)	107.00 ±17.62	78.00 ± 6.63	< 0.001
PPBS (mg/dl, mean ± SD)	166.63 ±21.99	114.83 ± 6.69	< 0.001
HBA1C (%,mean ± SD)	6.69 ±1.16	5.75 ± 0.46	< 0.001
Cesarean delivery (No., %)	40 (66.7%)	30 (50%)	0.064
GA at termination (wks, mean ± SD)	36.45 ± 0.746	36.20 ± 0.879	0.096
Neonatal birth weight (g,mean ± SD)	3315.17±455.41	3116.83±214.99	0.003
Neonatal blood sugar (mg/dl,mean ± SD)	68.27±22.07	79.92±18.83	0.002
1 min Apgar score (mean ± SD)	6.73 ± 1.039	7.47 ± 0.965	< 0.001
5 min Apgar score (mean ± SD)	8.08 ± 1.43	8.77 ± 1.17	0.005

Table (2): Frequency of adverse neonatal outcomes in study and control groups

Variable	Study group	Control Group	P value
Hypoglycemia (<50mg/dl - No., %)	14 (23.3 %)	2 (3.3%)	0.001
1 min Apgar score <7 (No., %)	18 (30%)	6 (10 %)	0.006
5 min Apgar score <7 (No., %)	12 (20%)	4 (6.7%)	0.032
NICU admission (No., %)	7 (11.7%)	3 (5 %)	0.186

Table (3): Gestational age at Doppler studies, Ultrasonographic findings & Doppler indices in study & control groups.

Variable	Study group	Control Group	P value
GA at Doppler study (wks, mean ± SD)	36.28±0.88	36.12 ±1.01	0.338
Macrosomia (No., %)	15 (25%)	2 (3.3%)	0.001
Polyhydramnios (No., %)	14 (23.3%)	4 (6.7%)	0.011
UA RI (mean ± SD)	0.63 ± 0.07	0.61 ± 0.06	0.057
UA PI (mean ± SD)	0.93 ± 0.25	0.95 ± 0.13	0.659
MCA RI (mean ± SD)	0.8 ± 0.1	0.83 ± 0.06	0.07
MCA PI (mean ± SD)	1.73 ± 0.45	1.81 ± 0.37	0.322
MCA/UA PI (mean ± SD)	1.94 ± 0.42	1.92 ± 0.29	0.754

Table (4): Patients characteristics and laboratory parameters, pregnancy characteristics and neonatal outcome in controlled and Uncontrolled diabetics groups.

Variable	Controlled DM	Uncontrolled DM	P value
Maternal Age (Y, mean ± SD)	30.53 ± 6.91	30.37 ± 4.55	0.913
BMI (kg/m^2, mean ± SD)	30.8 ± 4.506	29.93 ± 4.464	0.457
Primigravidas (No., %)	10 (33.3 %)	2 (6.7 %)	0.01
FBS (mg/dl, mean ± SD)	97.17 ± 13.24	116.83 ±16	< 0.001
PPBS (mg/dl, mean ± SD)	158.33 ± 23.50	174.93 ±17.01	0.003
HBA1C (%, mean ± SD)	5.95 ± 0.49	7.43 ±1.16	< 0.001
GA at termination (wks, mean ± SD)	36.37 ± 0.928	36.53 ± 0.507	0.393
Cesarean delivery (No., %)	16 (53.3%)	24 (80%)	0.028
Neonatal birth weight (g,mean ± SD)	3230.83± 322.86	3400.33± 550.18	0.150
Neonatal blood sugar (mg/dl, mean ± SD)	68± 22.03	68.53± 22.47	0.926
1 min Apgar score (mean ± SD)	6.77 ± 1.104	6.7 ± 0.988	0.806
5 min Apgar score (mean ± SD)	8.2 ± 1.448	7.97 ± 1.426	0.532

Table (5): Frequency of adverse neonatal outcomes in controlled and Uncontrolled diabetics groups.

Variable	Study group	Control group	P value
Hypoglycemia (<50mg/dl - No., %)	6 (20%)	8 (26.7 %)	0.542
1 min Apgar score <7 (No., %)	8 (26.7%)	10 (33.3%)	0.573
5 min Apgar score<7 (No., %)	5 (16.7%)	7 (23.3%)	0.519
NICU admission (No., %)	3(10%)	4 (13.3%)	1

Table (6): Gestational age at Doppler studies, Ultrasonographic findings & Doppler indices in controlled and Uncontrolled diabetics groups.

Variable	Controlled DM	Uncontrolled DM	P value
GA at Doppler study (wks, mean ± SD)	36.2 ±1.06	36.37±0.67	0.471
Macrosomia (No., %)	7 (23.3%)	8 (26.7%)	0.766
Polyhydramnios (No., %)	6 (20%)	8 (26.7%)	0.542
UA RI (mean ± SD)	0.62 ± 0.06	0.64 ± 0.08	0.5
UA PI (mean ± SD)	0.92 ± 0.23	0.94 ± 0.26	0.764
MCA RI (mean ± SD)	0.81 ± 0.09	0.79 ± 0.1	0.52
MCA PI (mean ± SD)	1.77 ± 0.45	1.69 ± 0.45	0.488
MCA/UA PI(mean ± SD)	1.98 ± 0.37	1.9 ± 0.47	0.46

Table (7): The sensitivity, Specificity, positive and negative predictive values and accuracy of umbilical artery & middle cerebral artery Doppler in the prediction of adverse neonatal outcomes among diabetic patients

	Umbilical artery Doppler		Middle cerebral artery Doppler	
Statistic	**Value**	**95% CI**	**Value**	**95% CI**
Sensitivity	25%	9.77% to 46.71%	20.83%	7.13% to 42.15%
Specificity	88.89 %	73.94% to 96.89%	91.67 %	77.53% to 98.25%
PPV	60 %	32.09% to 82.64%	62.50%	30.49% to 86.36%
NPV	64 %	57.86% to 69.71%	63.46 %	58.04% to 68.56%
Accuracy	63.33%	49.90% to 75.41%	63.33%	49.90% to 75.41%

PPV = Positive Predictive Value – NPV=Negative Predictive Value

Table (8): Logistic regression to detect independent predictors of cases

		P value	OR	95% C.I.	
				Lower	Upper
Cases	**Age (yrs)**	0.759	0.969	0.794	1.184
	FBS	0.147	1.183	0.943	1.484
	PPBS	0.018	1.319	1.049	1.659
	HBA1C	0.594	0.504	0.040	6.270
	Neonatal birth weight	0.377	0.998	0.993	1.003
	Neonatal blood sugar	0.300	0.960	0.890	1.037
	Apgar score at 1 min	0.486	0.496	0.069	3.557
	Apgar score at 5 min	0.539	0.610	0.126	2.952

Table (9): Correlation analysis of umbilical artery & middle cerebral artery Doppler indices with neonatal outcome

		RI (umbilical artery doppler)	PI (umbilical artery doppler)	RI (middlle cerebral artery)	PI (middlle cerebral artery)
Apgar score at 1 min	Correlation Coefficient	-0.073-	-0.073-	-0.033-	-0.035-
	P value	0.577	0.580	0.802	0.791
	N	60	60	60	60
Apgar score at 5 min	Correlation Coefficient	-0.141-	-0.141-	0.071	0.067
	P value	0.284	0.281	0.589	0.612
	N	60	60	60	60
Neonatal blood sugar	Correlation Coefficient	-0.123-	-0.120-	0.126	0.126
	P value	0.348	0.359	0.337	0.336
	N	60	60	60	60