# Predicting pregnancy outcome by Doppler study evaluation of fetal middle cerebral artery, umbilical artery and ductus venosus

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## Abstract

**Objective:** To investigate the sensitivity and specify of MCA, UA and DV Doppler pulsatility index as a diagnostic value for antepartum assessment of fetal wellbeing and prediction of adverse perinatal out come in both low and high-risk pregnancies.

**Patients and methods:** Aprospective observational case control study conducted at Mansoura university hospitals from February 2018 through march 2019 and involved 100 pregnant ladies with a singleton pregnancy divided into two equal groups, G1 cases with high risk pregnancy, and G2 cases with low risk pregnancy as a control group. Both groups were matched for age, parity and gestational age.

**Results:** The basic socio-demographic characteristics of the studied cases and controls were similar in age, gravidity, parity and body mass index ($p > 0.05$) but in G1 cases had significantly higher frequencies of mean systolic blood pressure, gestational hypertension, gestational DM, mild or severe PET, oligo- hydraminions, IUGR ($p < 0.001$). Despite there was no significant difference among cases and control as regard mean (SD) of gestational age in weeks, BPD (mm), UA PI ($p > 0.05$), but there is a highly significant difference as regard FL (mm), AC (mm), MCA PI, DV PI (p values $< 0.05$). Also; there is a significant difference regarding the reactivity of NST being more reactive in control than cases (35 vs 2, $p < 0.001$). Again; there is a significant difference between cases and control regarding mean (SD) of gestational age at delivery (34±2 vs 39±1 in G2, $p < 0.001$), Fetal weight (gm) (2255±1047 vs 2944±976, $p < 0.001$), Agar score at 5 minutes (4.9±1.1 vs 8.3±1.4, $p < 0.001$), occurrence of hypoxia (68% vs 2%, $p < 0.001$), need for NICU admission (66% vs 2% $p < 0.001$) and acidotic cord blood with PH < 7.2 (33 cases vs 1 case only, $p < 0.001$). Logistic regression analysis revealed the cut off value MCA PI (1.62) had high sensitivity (82%), specificity (78%), PV(79%), NPV (81%) and a diagnostic accuracy of (80%). Also, UA PI cut off value was found (1.12) with sensitivity (60%), specificity (68%), PPV(65%), NPV (63%) with a diagnostic accuracy of (64%). Regarding the best cut off value of DV study by the same method, DVPI cut off value was(0.77), with sensitivity (84%), specificity (80%), PPV(80%), NPV(83%) with diagnostic accuracy (82%).

**Conclusions:** Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being thus yielding an opportunity to improve fetal and neonatal outcome.

**Keywords:** Doppler, pre-eclampsia, gestational hypertension.

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## Introduction

During the first and second trimester, an ultrasound examination is used to screen the fetal malformations and assess the fetal growth disorders, a problem which is commonly encountered in pregnancy associated medical disorders namely, diabetes, pre-eclampsia, hematological diseases, cardiac problems and many others with a resultant maternal morbidity and premature iatrogenic deliveries[1]. Doppler ultrasound has emerged as a beneficial tool in the assessment of the fetal and placental circulation thus helping for prediction of adverse pregnancy outcome as the obtained data has been identified to decrease the figure of emergency operations, hospital admissions, and hospital stay for both the mother and the newborn especially with cases of suspected intrauterine growth restriction (IUGR)[2, 3]. Also, recent findings aided in timing delivery of severely growth-restricted fetuses by promoting the use of ductus venosus (DV) Doppler study. [4]. Additionally; Doppler investigation of middle cerebral artery (MCA) in combination with umbilical artery (UA) seems to improve prediction of adverse outcome in near-term pregnancies [5]. Therefore; it is postulated that Doppler ultrasound study for fetal circulations would be a useful addition to the obstetrician catalog of tests for antenatal fetal well-being and timely intervention that might be effective in reducing mortality and major morbidity in high-risk pregnancy [4]. The present study was held aiming for evaluation of the fetal MCA, UA and DV Doppler study for prediction of pregnancy outcomes in cases with high risk pregnancy.

## Patients and methods

This study is a prospective clinical case control study conducted at Department of Obstetrics and Gynecology, Mansoura University Hospitals, Egypt, from February 2018 to march 2019. Local institutional research board approval for the study was obtained with IRB number [17.02.02] together with a written and verbal informed consent from all the participant after clearly explaining the nature of the study, its health benefits, possible side effects and expected complications. Therefore, the study was performed in accordance with the ethical standards laid down with the Helsinki Declaration at 1975, as revised in 1983and its later amendments. This study is prospective observational study that carried out at Mansoura university hospitals to pregnant ladies with singleton pregnancy which serially selected and divided into two groups (50 control group & 50 high risk pregnancy women) both were matched for age, parity, gestational age. The number of allocated cases selected according the formula; (N =Z2P (1 - P)d2) used by Daniel, 1999 [6].Inclusion criteria included those at gestational age from 28-34 weeks as confirmed by sure due date or TAS, viable singleton pregnancy, diagnosed as high-risk pregnancy (e.g. PET, DM, heart disease, …. etc.), not using medication during pregnancy apart from iron supplements. Those having multiple pregnancies, placenta previa, fibroid, fetal congenital anomalies, auto immune or vascular disorders, history of nicotine use, alcoholism were excluded. Those in the control group exhibited apparently normal pregnancy. Patients' basic characteristics in both groups including full detailed history together with data obtained by examination, whether general or abdominal are collected and tabulated. Subsequently, trans-abdominal ultrasound was performed for all patients in both groups while in a slightly tilted position with the head raised 30 degrees and with a small pillow under the right loin using Samsung H60 ultrasound machine with Doppler unit and a convex linear transducer (3-5 MHz)and all cases were investigated by the same sonographer. Biometric measurement to assess gestational age, fetal growth through the determination of the fetal biparietal diameter, abdominal circumference and femur length were held and recorded. Measurement of the BPD was obtained at the level of the thalamus and cavum septum pellucidum meanwhile, the abdominal circumference was obtained from the junction of the umbilical vein and the lateral left portal vein. Estimated fetal weight was detected using the head, abdominal and femur measurements [7].On measuring umbilical artery Doppler, the uterine contents are scanned to select an area of amniotic cavity with several loops of umbilical cord, then using a pulsed wave Doppler on a free loop of cord, the characteristic sound and shape of the umbilical artery identified [8].When the screen showed at least 3 consecutive wave forms of similar height, the image was frozen and UA Doppler pulsatility index (PI), resistance index (RI), systolic/diastolic ratio (S/D)were estimated and recorded. Middle cerebral artery Doppler (MCA) was measured by standardizing aplan for measuring the biparietal diameter which includ-

ed the thalamus and cavum septum pellucidum, then the color and flow mapping function was then superimposed as the middle cerebral artery seen pulsating at the level of the origin of the circle of Willis. When the screen showed at least three consecutive wave forms of similar height, the image was frozen and MCA PI, RI and S/D were also estimated. Care was taken to apply minimal pressure by the transducer on the maternal abdomen as fetal head compression can alter fetal intracranial pressure and hence the arterial flow velocity wave forms. Ductus venosus (DV) Doppler was estimated by identifying the DV using two-dimensional and color Doppler imaging in a mid-sagittal section or oblique transaction of the fetal abdomen. The sample volume was placed in the distal smallest portion of the vessel in order to record the highest blood velocities and to avoid interference from blood flow in the IVC. The ductus venosus blood velocity waveform was a peak velocity during systole (S), end-systolic blood velocity (ES), peak velocity during diastole (D) and velocity corresponding to atrial contraction (A) The DV S/A-ratio was calculated and related to the normal reference value [9]. It is noted that all ultrasound recordings were obtained during periods of fetal apnea and quietness with absent movements while the mother is normoglycemic. All patients in both groups were followed up till delivery, then the mode of delivery and neonatal outcome were recorded and tabulated. All neonates were subjected to Apgar scoring after 1 and 5 minutes by an expert neonatologist attending delivery. Adverse neonatal outcome is considered when Apgar score is less than 7 at 5 minutes according to Caseyet al., 2001[10],neonatal admissions to intensive care units, fetal death either intrauterine or early after birth or cord blood sample PH showed acidosis i.e. pH less than 7.25[11].

## Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 17 for Windows® (SPSS Inc, Chicago, IL, USA). Qualitative data was presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data was presented as mean ± SD. F-test (One Way Anova) was used to compare between more than two groups. $P < 0.05$ was considered to be statistically significant. Independent-samples t-test of significance was used when comparing between two means. Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters. Receiver operating characteristic (ROC curve) analysis was used to find out the overall predictivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.

## Results

The basic socio-demographic characteristics of the studied cases and controls are shown in Table 1. Both groups were similar in age, gravidity, parity and body mass index ($p > 0.05$). Compared to controls, women in G1 (cases) had significantly higher frequencies of mean systolic blood pressure (145.4±20.2 vs 105.7±17.6, $p < 0.001$), newly developed gestational Hypertension, gestational DM, per-eclampsia (mild or severe), oligo- hydraminions, IUGR or combined severe preeclampsia, oligo- hyarminions & IUGR ($p < 0.001$), table [1].

Data showing comparison of fetal and neonatal characteristics in both groups were presented in table 2. Despite there was no significant difference among cases and control as regard mean (SD) of gestational age in weeks at examination, BPD (mm), UA PI (31±2.2 vs 31±2.3, 84.86±17.63 vs 85.21±15.42, 1.19±0.43 vs 1.37±0.24, $p > 0.05$), but there is a highly significant difference as regard FL (mm), AC (mm), MCA PI, DV PI (51.17±11.46 vs 62.03±9.60, 203.44±87.13 vs 268.53±99.62, 1.22±0.31 vs 1.94±0.33, 0.84±0.48 vs 0.70±0.23 respectively, p values $< 0.05$). Also; there is a significant difference regarding the reactivity of non-stress test being more reactive in control than cases (35 vs 2, $p < 0.001$).Again; there is a significant difference between cases and control regarding mean (SD) of gestational age at delivery (34±2 vs 39±1 in G2, $p < 0.001$), Fetal weight (gm) (2255±1047 vs 2944±976, $p < 0.001$), Agar score at 5 minutes (4.9±1.1 vs 8.3±1.4, $p < 0.001$), occurrence of hypoxia (68% vs 2%, $p < 0.001$), need for NICU admission (66% vs 2% $p < 0.001$) and acidotic cord blood with PH < 7.2 (33 cases vs 1 case only, $p < 0.001$), table [2].Receiver operating characteristics (ROC curve) analysis in table (3) was used to define the best cut off value of MCA

PI and revealed the cut off value 1.62 had high sensitivity(82%), high specificity (78%), positive predictive value 79%, negative predictive value of 81% and this means a valuable diagnostic accuracy of 80%. Also, in table (3) ROC curve study for UA showed that UA PI at the cut off value 1.12 with sensitivity 60%, specificity 68%, positive predictive value 65%, negative predictive value 63% with diagnostic accuracy of 64%. Regarding the best cut off value of DV, the same method used showed that DVPI cut off value 0.77, with sensitivity of 84%, specificity 80%, positive predictive value 80%, negative predictive value 83% with diagnostic accuracy 82%, table [3].

## Discussion

To our knowledge, no previous data had been published from our locality on Doppler study involving UA, MCA and DV PI and S/D ratios for predicting the outcome of high-risk pregnancies. There are many researches performed involving each parameter separately but results from our study confirmed the fact that; studying DV PI had highest sensitivity (84%), negative predictive value (83%) and a valuable diagnostic accuracy (82%).

It is well known that Doppler study in obstetrics is largely used to examine the vascular system as the elevated impedance to blood flow in the placenta is reflected by abnormal umbilical artery velocimetry with subsequent placental insufficiency and fetal growth restriction but this may be associated with a change in the fetal cerebral waveforms suggesting increased blood flow to the brain [1, 12]. However, an abnormal umbilical artery signal and the brain-sparing effect do not necessarily predict the outcome in growth-restricted fetuses. Recently, more attention has been paid to the venous system as umbilical vein pulsations and reversed flow in the ductus venosus as threatening signs of perinatal mortality [13] as the ductus venosus is considered as the only direct link between the inferior vena cava and the umbilical vein[14]. Few studies have evaluated the fetal MCA, UA and ductus venosus Doppler study for prediction of pregnancy outcomes as stated by Gardosi, et al., 2018 [15].

Our study results regarding preliminary ultrasonography data showed that patient's group had statistically significant lower FL, AC than those of control group and this comes in agreement with data proved by some authors [16, 17].

The clinical findings of the study cohort demonstrated that patients group displayed lower statistically significant reactive non-stress than control group ($p < 0.001$) and this came in agreement with those proved by Garg, et al., 2016 [18]but contrary to Verma, et al., 2015 [19]who verified the predicting value of NST for fetal compromise is negligible. In our patients, the gestational hypertension represented the highest percentage of risk factors while gestational DM and Mild per- eclampsia had nearly equal prevalence, severe per- eclampsia displayed the 4thrisk factor rank, Oligo-hydraminions, IUGR and Severe PET, oligo- hyarminions & IUGR come as last. These results came in agreement with many authors [20-22] but not in agreement with some others [23-25] who reported that the incidence of GDM to be first and the overall incidence of gestational hypertension to be as low as 5.9% with annual fluctuations.

Also, the results obtained by the current study indicated significant differences between patients and controls group regarding MCA and DV Doppler ultrasound and this came in consistent with Turan, et al, 2008 who identified the sequence of progression of arterial and venous Doppler abnormalities from the onset of placental insufficiency in IUGR. In other words, our Doppler indices gained by studying multiple vessels in the feto placental circulation can help in the monitoring of compromised fetus, predicting neonatal morbidity and useful in determining the optimal time of delivery in complicated pregnancies, a notion which is recently proved by some researchers [1, 26, 27].

Again; our study proved a statistically significant difference between patients and healthy group regarding gestational age at delivery, being shorter in patients than control, lower fetal weight, lower average Apgar core with more need for NICU as well as more acidotic blood and hypoxia, the findings which stated before by li, et al., 2013 and Harper, et al., 2016 [29, 30]. Despite our research verifies the advantage of studying multiple vessels in the placental and fetal circulations simultaneously for governing the pregnancy and neonatal outcome but indeed it has some drawbacks. First, it is a uncenter study involving only 100 patients and actually this is a relatively low number in

comparison to the total number of high risk pregnancy seen, booked, followed up in a tertiary care hospital likeours, so the authors advice for a large multicenter study for the results to be more convenient, appropriate and impressive. Second, the neonatal outcome recorded in our results depend only on the short period follow up for the first day and later follow up records, including early or late deaths or even short term morbidities, were missed as this point was the concern of neonatologist thus adding a point of weakness to our work.

## Conclusion

Doppler velocimetry studies of placental and fetal circulation can provide important information regarding fetal well-being, yielding an opportunity to improve fetal outcome.

**Conflict of interest**: no conflict of interest to be declare.

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