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" Neonatal outcome among High Risk Pregnant Women depending on the ratio of Fetal Cerebroplacental Artery versus Uterine Artery Doppler Ultrasonography "

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ABSTRACT:

Background: Doppler velocimetry was used to investigate the typical physiological vascular changes that take place within the placenta and the fetus and application of these changes to predict high risk pregnancy and perinatal outcome.

Aim and objectives: to evaluate neonatal outcome among high risk pregnant women depending on fetal cerebroplacental ratio (CPR) versus uterine artery (UtA) Doppler.

Subjects and methods: This current study was a prospective randomized control trial which was conducted at ElShatby Maternity University Hospital from January 2021 to December 2022 after being approved by the Faculty of Medicine- Port-said University ethical committee on 119 singleton high risk pregnancies which were distributed at random into group A who were evaluated by CPR and group B who were evaluated by UtA.

Results: In current study there was a statistically significant difference between the studied groups regarding fetal CPR Doppler ultrasonography, comparison of neonatal characteristics except in infant sex and neonatal outcome. APGAR score at 5th min, CPR ,middle cerebral artery (MCA) PI(pulsatility index), MCA peak systolic velocity(PSV) have statistically significant positive correlation with birth weight while umbilical artery (UA) PI, umbilical cerebral ratio (UCR), UtA PI and UtA resistance index (RI) have statistically significant negative correlation with birth weight.

Conclusion: In high risk pregnancies, the CPR and UtA Doppler have a significant impact on the ability to predict the fate of the perinatal period.

Keywords: Cerebroplacental, Uterine Artery, Doppler Ultrasonography, Neonatal outcome

Introduction :

Doppler flow fetal hemodynamic status assessment is increasingly being used to predict high risk pregnancies that may result in adverse fetal outcomes by providing information beyond ultrasound-based fetal growth assessment alone **(1, 2)**.

The uterine artery (UtA) blood flow among the uterus and the placenta may be monitored with Doppler ultrasound (US). In the nongravid condition, the waveform exhibits high resistance, characterized by low diastolic flow and an early diastolic notching. The UtA branches need to be redesigned so that the waveform has low resistance with continuous diastolic flow in order for placentation to take place normally. During pregnancy, the UtA generates a low impedance flow due to trophoblastic invasion. Preeclampsia, placental abruption, intrauterine fetal growth restriction (IUGR), and stillbirth are some of the maternal and newborn consequences of failing to do this **(3)**.

Higher chances of adverse perinatal outcomes were predicted by the Doppler markers as abnormal fetal-brain Doppler indices & placental underperfusion **(4, 5)**. As a result, in cases of suspected abnormal neonatal outcome , UtA Doppler, along with cerebroplacental ratio (CPR), umbilical artery (UA) Doppler, and expected fetal weight (EFW), has been proposed as a predicting tool for identifying risky ones **(6, 7)**.

The aim of our work was to evaluate neonatal outcome among high risk pregnant women depending on the CPR versus UtA Doppler Ultrasonography.

Patients and Methods:

This current prospective randomized control trial was conducted on 119 pregnant women from January 2021 to December 2022 at ElShatby Maternity University Hospital after being approved by the Faculty of Medicine- Port-said University ethical committee

Study population:

I. All high-risk pregnant ladies with those **inclusion criteria** were eligible as following A**:** a singleton pregnancy.

B: chronic hypertension, uncontrolled diabetes, systemic lupus, antiphospholipid syndrome, renal diseases, vasculopathy and metabolic disorders

C: past history of IUGR.

II. Those of low-risk pregnant ladies were **excluded** in addition to those with multiple gestations, documented major congenital abnormality, aneuploidy or genetic syndrome congenital infection were excluded as well.

Sample size:

Based upon a previous study aimed to assess the diagnostic performance of fetal MCA and UA by Doppler ultrasonography in high-risk mothers and association with perinatal consequence the required minimal sample size was calculated. **Malik and Saxena (8)** concluded combined use of both UA and MCA Doppler study including the CPR increase the sensitivity of the Doppler studies for prediction adverse perinatal outcome.

Based on their findings, sample size of 119 pregnant women was the enough required sample to conduct this diagnostic test accuracy study, assuming a level of significance 95% (α=0.05), and statistical power (1

– β) of 90%, with assumption of discrimination power of Doppler PI in pregnant women is 70% area under the ROC curve **(9)**.

Randomization:

Those risky patients eligible to current study participated after giving a written informed consent regarding the methodology & objective of the study. They were randomly allocated into either: group A (those who were undergone CPR evaluation) or group B (those who were undergone UtA Doppler evaluation) using computer-generated randomization

Each participant was allocated into either one of the two groups using simple random sample, 1:1 randomization in which computerized random sample was taken from study population. Each one received a sealed envelope provided to the patient by the nurse in the outpatient clinic.

The current study was started on those eligible patients at 20 **weeks** gestational age pregnancy when all risky patients were evaluated thoroughly about :

I. The pregnant lady age

II. Gestational age (GA) was determined using Negele's rule in case of reliable menstrual cycle **(10)** in addition to the crown rump length (CRL) in the first trimester .If not conducted ;head circumference(HC) with or without femur length(FL) can be carried out from second trimester **(11)**.

III. Obstetric history: Gravidity & Parity (duration of each pregnancies, deliveries methods, outcome of each pregnancy as regards fetal sex , weight ,intensive care unit (ICU) admission & complications if any)

IV. Past history regarding medical history as: hypertension, uncontrolled diabetes, systemic lupus, renal diseases, vasculopathy and metabolic disorders as well as surgical history

V. Any laboratory investigations if they have (fasting blood glucose (FBG), post prandial glucose level, glycosylated HbA1C, blood urea nitrogen (BUN), serum creatinine, albumin: creatinine ratio)

Each group was evaluated then (after being randomly allocated to either one):

Group **A**; whom were evaluated by obtaining UA pulsatility index (PI) & middle cerebral artery (MCA) PI to calculate the **CPR (12)** by dividing mean MCA PI by mean UA PI assuming that cutoff value of CPR 1 or more as normal while ≤ 1 as abnormal.

(The MCA PI **(13)** is calculated by dividing the peak systolic velocity (PSV) minus the end-diastolic velocity (EDV) by the time-averaged velocity (TAV) PI = (PSV - EDV) / TAV

UA Doppler **(14)** were obtained at **24-28** weeks of gestation for each patient in a free floating umbilical cord loop in which flow resistance is intermediate.

In addition **MCA** was recorded in the circle of Willis cross sectionally in the absence of fetal movement or uterine contractions keeping the angle of insinuation at less than 30 degrees **(15)**

A mean value of least 3 consecutive waveforms of UA and MCA PI was recorded.

Group **B**: was assessed by recording the **UtA** Doppler from its origin in the internal iliac artery (IIA) in the lateral pelvic wall over the iliac fossa and tracking its course. Pulsed Doppler was then administered 1 cm medially, at an angle of insinuation of less than 30 degrees, at the point of passing over the external iliac artery (EIA); The PI to be obtained both left and right by measuring mean value of three similar consecutive waveforms **(16)**, (taking into consideration the placental side). UtA Doppler measurement was said to be abnormal if any of the following is present: notching, PI >95th percentile or ≥2 standard deviation (SD) above the mean, RI > 0.50, or any abnormal waveform. Each patient was first evaluated at **20–24** weeks of gestation.

Ultrasound and Doppler studies were performed using Mindray DC 70 ultrasound systems and 3-7 MHz probes.

Then all those eligible ladies (i.e .both groups) were followed & were assessed through :

-Serial ultrasound estimation of **fetal weight** using **Hadlock's formula (17)** every two weeks. Those obtained values were converted into centiles **(18) .** Taking those fetuses who are **less than 10th** percentile & diagnosed **after 32** weeks to be late onset intrauterine growth restricted.

-In addition to further parameters which were evaluated postnatal as: mode of delivery (emergency cesarean section(cs) due to fetal distress), fetal hypoxemia as detected by pH of umbilical artery **(19)**,Pulse oximetry and APGAR score **(20)** at 1, 5 and 10 minutes . The score was recorded at 1 minute and 5 minutes in all infants with expanded recording at 5-minute intervals for infants who score seven or less at 5 minutes, and in those requiring resuscitation as a method for monitoring response. Scores of 7 to 10 are considered reassuring, neonatal special care unit admission, fetal sex as well as its birth weight.

Statistical analysis:

The acquired data was evaluated, and a manual coding process was applied. The Statistic Package for the Social Sciences, Version 22 (SPSS 22) for Windows, was employed to do statistical analysis on these numerical codes.

Descriptive statistics: Quantitative data and Qualitative data

Analytical statistics: Comparing groups was done via Chi square-test (X^2), Student's "t"- test, Mann Whitney test, ANOVA test, Pearson correlation, Stepwise linear logistic regression analysis and Receiver operating characteristic curves (ROC)

The coefficient interval was set to 95%. The level of significance was calculated according to the following probability (P) values: $P<0.05$ was considered statistically significant.

The coefficient interval was set to 95%. The following P values determined significance: $P<0.05$ was statistically significant, $P<0.001$ was highly significant and $P>0.05$ was non-significant.

Results:

Among current studied pregnant females; 69.7% were primigravida and 30.3% were multipara; their age ranged between 18-38 years. 68.1% were born via caesarean section (CS). 50.4% have hypertension (HTN), 22.7% have pregestational diabetes millets (DM), 11.8% have systemic lupus erythromatosis (SLE), 5.9% have chronic kidney disease (CKD), 5% have anti-phospholipid $, while 4.2% have vasculopathy. At the time of assessment GA ranged between 32-33 weeks and fetal weight ranged between 1123 – 1476 gm. **[Table 1]** and **(figure 1).**

There was a statistically significant difference between the two studied groups regarding UA PI, MCA PI, umbilical cerebral ratio (UCR), CPR and PSV. **[Table 2]**

There was a statistically significant difference between the two studied groups regarding GA at birth (weeks), Birth weight (gm), APGAR at 5^{th} and NICU admission. There was no statistically significant difference between the two studied groups regarding infant sex. **[Table 3]**

There was a statistically significant difference between the two studied groups regarding comparison of neonatal complications. **[Table 4]**

There was a statistically significant difference between the two studied groups regarding comparison of neonatal outcome. **[Table 5]** and (**figure 2).**

APGAR score at 5th min, cerebroplacental ratio, MCA PI, MCA PSV have statistically significant positive correlation with birth weight while UA PI, umbilical cerebral ratio (UCR), UtA PI, UtA resistance index (RI) have statistically significant negative correlation with birth weight. **[Table 6]**

Discussion:

Analysis of current findings revealed that as regard maternal data; 69.7% were primigravida and 30.3% were multipara; their age ranged between 18-38 years. 68.1% were born via CS. 22.7% have Pre_gestational DM, 50.4% have HTN, 11.8% have SLE, 5.9% have CKD, 5% have anti-phospholipid syndrome, while 5% have vasculopathy. At the time of assessment GA ranged between 32-33 weeks and fetal weight ranged between 1123 – 1476 gm.

In agreement with current findings, the study of **Prajapati et al., (21)** on 400 high risk women revealed that there were 375 people in the age bracket of 20–30 years, with the mean age ± standard deviation of research participants being 25 ± 3.3 years. Anemia accounted for 67 (16.75%) of the problems that occurred during the most recent pregnancy, whereas hypertension caused 15 (3.75%) of the cases & diabetes caused 11 (2.75%).

In the present study, as regard neonatal outcomes; 65.5% were born preterm, and 34.5% were full term

-. Birth weight ranged between 1273-2076 gm. 58% of them were IUGR while the remaining 42% were of normal weight. 51.3% of them need NICU admission and 52.1% develop complications. The commonest complications were hypoglycemia (14.3%), respiratory distress syndrome (RDS) (12.6%),persistent pulmonary hypertension (PPHN) (9.2%), bronchopulmonary dysplasia (BPD) (7.6%), hypoxic ischemic encephalopathy (HIE) (5%) and meconium aspiration (3.4%). Most of neonates have survived 66.4% with 25.2% neonatal death and 8.4% were still birth.

In comparison with current findings, the study of **Gleason et al., (22)** determined that neonates of high risk women were 1.34 times more likely to be delivered by caesarean section as opposed to vaginal delivery. They were also 1.77 times more likely to deliver pre-term at under 37 weeks, as well as had an almost 2-fold elevated risk of all pre-term birth categories, including extremely, very, and moderate to late pre-term. In addition to this, they were more probable to have a low birth weight (less than 2500 grams) and small for gestational age (SGA), whereas they were less likely to have a macrosomic birth weight (at least 4000 grams). The neonates born to mothers who had any type of disability had a shorter mean gestational age than those born to mothers who had no known handicap (37.6 weeks as opposed to 38.6 weeks), and their time spent in the NICU was much longer (11 days as opposed to 7 days).

Interestingly, in the current study, UA PI and umbilical cerebral ratio are statistically significant higher in IUGR than normal weight group. While, CPR, MCA PI, and MCA PSV are statistically significant lesser in IUGR than normal weight group.

In agreement with current findings, the study of **Coenen et al., (23)** It was observed that pregnancies impacted by FGR had a lower median CPR as well as conversely greater median UCR (1.17 vs. 1.62; p under 0.001; 0.86 vs. 0.62; p less than 0.001, respectively). This disparity can be linked back to the fact that FGR is identified by abnormal Doppler measurements.

In the current study ,Preterm birth and NICU admission are statistically significant higher in IUGR than normal weight group. While, Birth weight and APGAR at 5th min are statistically significant lower in IUGR than normal weight group. Neonatal complications are statistically significant higher in IUGR than normal weight group. There is statistically significant poor neonatal outcome in IUGR than normal weight group.

Consistent with current findings, the study of **Ouda et al., (24)** have found significant variations amongst all three groups with respect to GA and Apgar at five minutes.

In addition to above findings, in the current study; Stepwise linear regression analysis revealed that UA PI, UtA PI and MCA PSV are statistically significant independent predictors of IUGR.

In harmony with current findings, the study of **Liu et al., (25)** indicated that the UA-MDV, UA-TAMXV, UA-PSV, & UA-EDV decreased with the reduction of fetal weight among the FGR, SGA, as well as AGA groups. Analyses using multivariate logistic regression demonstrated that the UA-TAMXV was a significant independent factor in FGR prediction. It had a value for predicting FGR that was somewhere in the middle. The confidence interval for the area under the receiver operating characteristic curve was 0.79 to 0.85, and it was 0.82. On the other hand, in the present study APGAR score at 5th min, CPR, MCA PI, MCA PSV have statistically significant positive correlation with birth weight while UA PI, UCR, UtA PI, UtA RI have statistically significant negative correlation with birth weight

Najam et al., (26) compared to MCA Doppler, whose sensitivity, specificity, positive predictive value(PPV) and negative predictive value (NPV) for detecting IUGR were 59.25, 88.89, 72.72, as well as 81.35%, UA Doppler's sensitivity, specificity, PPV and NPV were 48.15, 80.67, 53.06 & 77.41%. C/U ratios of 85.18, 89.72, 80.70, and 92.30 are considered abnormal. Therefore, CPR has the highest PPV and is the most sensitive method for detecting IUGR.

Conclusion:

In high-risk pregnancies the CPR and UtA Doppler have a significant impact on the ability to predict the fate of the perinatal period.

Table (1): Descriptive maternal data of the studied population

		No.= 119
Parity	Primigravida	83(69.7%)
	Multipara	36(30.3%)
Maternal age (year)	Range	18 – 38
	Mean ± SD	26.49 ± 4.98
Mode of delivery	NVD	38 (31.9%)
	CS	81 (68.1%)
Maternal diseases	HTN	60 (50.4%)
	Pregestational diabetes	27(22.7%)
	SLE	14 (11.8%)
	Anti-phospholipid $	6 (5%)
	CKD	7 (5.9%)
	Vasculopathy	5 (4.2%)
BMI (kg/m^2)	Range	22 – 36
	Mean ± SD	25.89 ± 3.28
GA at assessment (weeks)	Range	32 - 33
	Mean ± SD	32.63 ± 0.48
Fetal weight at assessment (gm)	Mean ± SD	1290.81 ± 97.23
	Range	1123 – 1476

Table (2): Comparison of fetal CPR Doppler ultrasonography of the studied groups

		Group A	**Group B**	**t/x^2**	**P-value**	**Sig.**
		No.= 69	**No.=50**			
UA PI	Range	1.03 – 1.70	0.89 – 1.45	9.320 •	**<0.0001**	HS
	Mean ± SD	1.30 ± 0.18	1.04 ± 0.13			
MCA PI	Range	1.27 – 1.80	1.56 – 1.98	-7.935 •	**<0.0001**	HS
	Mean ± SD	1.52 ± 0.16	1.71 ± 0.10			
UCR	Range	0.49 – 1.23	0.51 – 0.87	8.399 •	**<0.0001**	HS
	Mean ± SD	0.85 ± 0.13	0.69 ± 0.07			
CPR	Range	0.83 – 1.96	0.83 – 1.98	-2.843 •	**0.005**	HS
	Mean ± SD	1.42 ± 0.28	1.57 ± 0.28			
MCA PSV	Range	40.50 – 59.00	48.00 – 64.5	-7.504 •	**<0.0001**	HS
	Mean ± SD	48.54 ± 5.03	54.57 ± 3.72			

Table (3): Comparison of neonatal characteristics of the studied groups

		Group A	Group B	t/x^2	P-value	Sig.
		No.= 69	**No.=50**			
GA at birth (weeks)	Preterm	60 (87%)	18 (20%)	8.710*	**0.003**	HS
	Full-term	9 (13%)	32 (80%)			
Infant sex	Male	39 (56.5%)	28 (56%)	1.819	0.178	NS
	female	30 (43.5%)	22 (44%)			
Birth weight (gm)	Range	1073 – 1490	1924 – 2976	-88.998•	**<0.0001**	HS
	Mean ± SD	1287.39 ± 53.32	2336.54 ± 75.33			
APGAR at 5th min	Range	3 – 9	6 – 9	-4.359•	**<0.0001**	HS
	Mean ± SD	7.54 ± 1.59	8.55 ± 0.72			
NICU admission	Yes	52 (75.4%)	9 (18%)	38.182*	**<0.0001**	HS
	No	17 (24.6%)	41 (82%)			

Table (4): Comparison of neonatal complications among the studied groups

	Group A	Group B	t/x^2	P-value	Sig.
	No.= 69	**No.=50**			
RDS	12 (17.4%)	3 (6%)	**17.415**	**<0.00001**	**HS**
PPHN	9 (13%)	2 (4%)			
hypoglycemia	14 (20.3%)	3 (6%)			
BPD	7 (10.1%)	2 (4%)			
Meconium aspiration	3 (4.3%)	1 (2%)			
HIE	5 (7.2%)	1 (2%)			
No complications	19 (27.5%)	38 (76%)			

Table (5): Comparison of neonatal outcome of the studied groups

		Group A	Group B	t/x^2	P-value	Sig.
		No.= 69	**No.=50**			
GA at birth (weeks)	**Death**	27(39.1%)	3 (6%)	25.352*	**0.0001**	HS
	Still birth	9 (13%)	1 (2%)			
	Survived	33 (47.8%)	46 (92%)			

Table (6): Correlation between the birth weight and clinical data of studied population

Variables	Birth weight	
	r	P-value
Maternal age (year)	0.025	0.784
Maternal BMI (kg/m^2)	-0.053	0.564
GA at birth (weeks)	-0.002	0.986
APGAR score at 5th min	0.373	<0.0001
UAPI	-0.604	<0.0001
MCAPI	0.527	<0.0001
UCR	-0.521	<0.0001
CPR	0.281	0.002
MCAPSV	0.558	<0.0001
UtAPI	-0.207	0.024
UtARI	-0.318	<0.0001

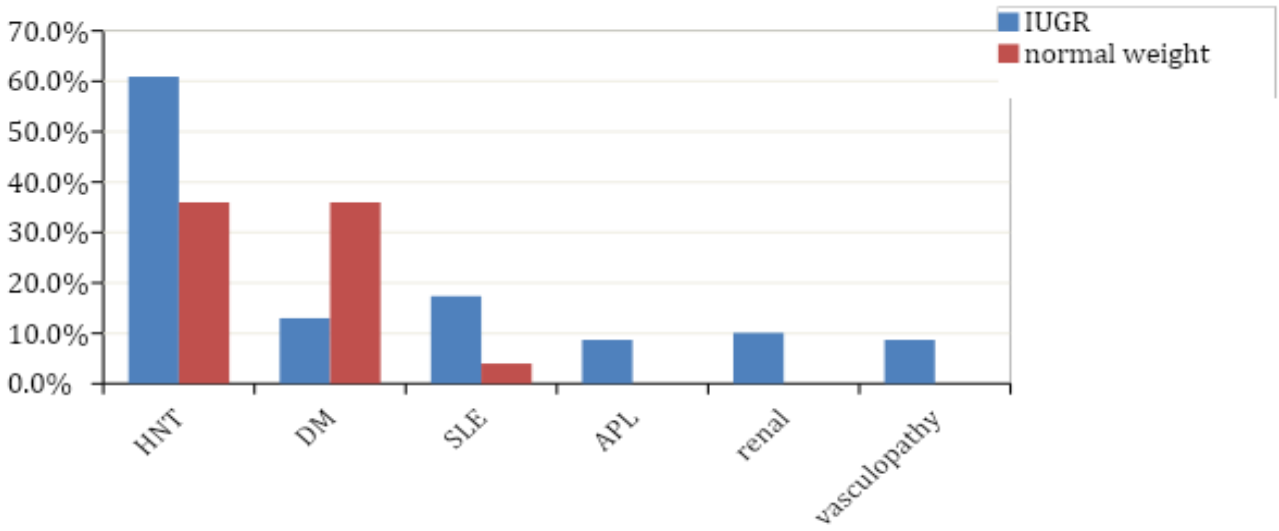

Figure 1: maternal diseases among the studied groups

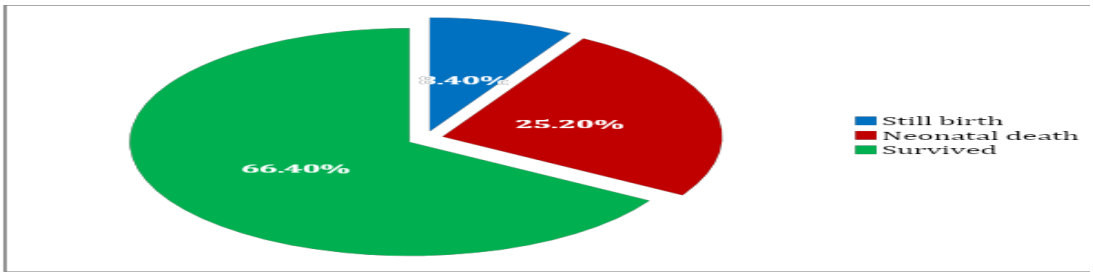

Figure 2: outcome of the studied neonates

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