

THE VALUE OF MIDDLE CEREBRAL TO UMBILICAL ARTERY DOPPLER RATIO IN THE PREDICTION OF NEONATAL OUTCOME AMONG WOMEN WITH PREGNANCY INDUCED HYPERTENSION

By

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ABSTRACT

Background: Hypertensive disorders complicating pregnancy are common and form one of the deadly triad, along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality.

Objective: To evaluate the role of middle cerebral artery and umbilical artery pulsatility index (PI) ratio in predicting neonatal outcome in pregnancies induced hypertension.

Patients and methods: This study which included 100 women with severe preeclampsia admitted to Alsayed Galal University Hospital during the period between November 2018 and July 2019. Were evaluated the accuracy of middle cerebral/umbilical artery pulsatility index ratio in predicting admission to neonatal intensive care unit (NICU), acidemia and low Apgar score at 5 minutes after birth in neonates of severe preeclamptic pregnant women.

Results: The best cut off value of middle cerebral artery (MCA) / umbilical artery (UA) PI ratio for prediction of NICU admission was sensitivity 62.5%, specificity 71.43%, positive predictive value (PPV) 29.41%, negative predictive value (NPV) 90.91% and the accuracy 70%. The cut off value of MCA/UA PI ratio for prediction of low Apgar score at 5 min was 50% sensitivity and 88.10% specificity. Estimated positive predictive value =44.44 and negative predictive value =90.24, and the cut off value of MCA/UA PI ratio for prediction of low UA PH were 43.75% sensitivity, 69.05% specificity, estimated positive predictive value =21.21, and negative predictive value =86.57.

Conclusion: Doppler data combining both umbilical and cerebral velocimetry provides information on consequences of the placental abnormality; Hence, Doppler can be a useful tool in the management of patients with preeclampsia and can help in deciding the time of delivery so that the fetus can be saved.

Keywords: Value of Middle Cerebral, Umbilical Artery Doppler Ratio, Prediction of Neonatal Outcome, Pregnancy, Hypertension

INTRODUCTION

There are four major hypertensive disorders that occur in pregnant women according to (*American College of Obstetricians and Gynecologists, 2013*):

1. **Preeclampsia-eclampsia** refers to the syndrome of new onset of hypertension and either proteinuria or end-organ dysfunction most often after 20 weeks of gestation in a previously normotensive woman. Eclampsia is

diagnosed when seizures have occurred.

2. Chronic (preexisting) hypertension is defined as systolic pressure ≥ 140 mmHg and/or diastolic pressure ≥ 90 mmHg that antedates pregnancy, it is present before the 20th week of pregnancy, or continues longer than 12 weeks postpartum.

3. Preeclampsia-eclampsia superimposed upon chronic hypertension is diagnosed when a woman with chronic hypertension develops worsening hypertension with new onset proteinuria or other features of preeclampsia (eg: elevated liver enzymes, low platelet count).

4. Gestational hypertension refers to elevated blood pressure first noticed after 20 weeks of gestation in absence of proteinuria or other diagnostic features of preeclampsia. Over time, some patients with gestational hypertension will develop proteinuria or end-organ dysfunction characteristic of preeclampsia and be considered preeclamptic, while others will be diagnosed with pre-existing hypertension because of persistent postpartum elevation of blood pressure.

Satisfactory development of uteroplacental and fetoplacental circulation is required for a normal pregnancy outcome. Alternative in its development can be associated with hypertension during pregnancy, which can lead to impaired circulation causing prematurity, subnormal growth (IUGR) or fetal death (*Smitha et al., 2014*).

Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels

has become established method of antenatal monitoring (*Srikumar et al., 2017*).

In preeclampsia, placental insufficiency due to increased vascular impedance is reflected by raised pulsatility index in the umbilical artery. Vasodilation of the cerebral arteries as compensatory mechanism to preserve adequate oxygen supply to brain is reflected by decreased pulsatility index in the cerebral arteries (*Varsha et al., 2013*).

Umbilical arteries are the common vessels assessed by Doppler ultrasound, but recent studies confirm the efficacy of middle cerebral artery (MCA) Doppler assessment and advocate it. Middle cerebral artery (MCA) Doppler measurement is a well-known modality for detecting fetal compromise. With the use of Doppler velocimetry, correct detection of compromised IUGR fetus is possible, which allows for timely intervention to improve perinatal outcome (*Gaikwad et al., 2018*).

The aim of this study was to evaluate the role of middle cerebral artery and umbilical artery pulsatility index ratio in predicting neonatal outcome in pregnancies induced hypertension.

PATIENTS AND METHODS

This study was a cohort study between women with severe preeclampsia. One hundred cases who were at 34 to 40 weeks of gestation with severe preeclampsia attended antenatal clinic and emergency room at Obstetrics and Gynecology Department, Faculty of Medicine, AlSayed Galal University Hospital during the period between November 2018 and July 2019, The ultrasound machine used

was Mindray Dc-N3, with a Doppler unit and a 3.5 MHz convex linear probe. The output power of 50mW/cm² was used, and the high-pass filter was set to 100Hz. Systemic random sample was used for selection of Cases.

All women were subjected to complete history, general examination, abdominal examination, and laboratory investigations (Complete blood picture, complete urine analysis, blood glucose fasting and postprandial, liver function test, renal profile, blood coagulation profile, prothrombin time, and ultrasonography).

Fetal middle cerebral artery and umbilical artery Pulsatility Index (PI) was calculated by subtracting the end diastolic velocity (**EDV**) from the peak systolic velocity (**PSV**) and then dividing by the time averaged (mean) velocity (**TAV**): $PI = (PSV - EDV) / TAV$. Every pregnant woman was subjected to only one examination to measure the fetal middle cerebral artery/umbilical artery pulsatility index ratio for measurement of cerebroplacental ratio. An axial view of the fetal head was obtained at the level of cerebral peduncles, then the color Doppler was used to visualize the circle of Willis, multiple middle cerebral artery were obtained and the average pulsatility index was used and Doppler sample volume was placed within 1 cm of the origin of the MCA that was easily identified as a major branch running anterolateral from the circle of Willis toward to the lateral edge of the orbit. UA Doppler evaluation was performed by sampling of a free-floating loop of umbilical cord and the PI was obtained. The angle between the

ultrasonographic beam and direction of blood flow is always <30 degrees. An abnormal CPR is defined as a CPR of less than 1 or a CPR below the 5th percentile for gestational age on the basis of the nomogram (*Baschat et al., 2013*).

Apgar score was determined at 5 minute after birth, Neonatal morbidity was established if:

1. Apgar score <7 at 5 minutes.
2. Neonatal acidemia of pH<7.2.
3. Newborn was admitted to the neonatal intensive care unit (NICU).

Statistical analysis:

The data were collected, coded, revised, verified, and computerized. Statistical analyses were done using SPSS statistical package version 16. (IBM Corp, Chicago, IL, USA) Qualitative data were presented in the form of numbers and percentages and quantitative variables as mean and standard deviation (SD). Sample size has been calculated using PASS® version 11 programs 6. It was estimated that a total sample (minor accepted) 100 women according to inclusion criteria, was required to achieve a power of 80 % (accepted margin of error 5%) and confidence level 95%, for detection of statistical significance as regards the correlation between 3rd trimester middle cerebral artery/umbilical artery Doppler parameters and neonatal outcome. Chi-square test (X^2), was used to compare qualitative variables. P-value <0.05 was considered statistically significant.

RESULTS

A total 100 pregnant women with severe preeclampsia were recruited in the study ,As regard the descriptive data of the patients characteristics, mean \pm SD of age was 28.620 ± 4.273 , As regards the parity of patients ,24(24%) were p0, 28

(28.0%) were p1, 26 (26%) were p2, 20(20%) were p3, 2(2%) p4, 64 of cases had no previous abortion, and mean \pm SD of gestational age was $36.240 (1.664)$ weeks (**Table 1**).

Table (1): Characteristics of the study population

Age (years)	Range	20-35
	Mean \pm SD	28.620 \pm 4.273
Gestational age (weeks)	Range	34-40
	Mean \pm SD	36.240 \pm 1.664
Parity (P)	P0 (No & %)	24(24.00%)
	P1 (No & %)	28(28.00%)
	P2 (No & %)	26(26.00%)
	P3 (No & %)	20(20.00%)
	P4 (No & %)	2(2.00%)
Previous abortions	Nil (No & %)	64(64.00%)
	One abortion (No & %)	24(24.00%)
	Two abortions (No & %)	12(12.00%)
Mode of delivery	CS delivery (No & %)	86(86.00%)
	Normal vaginal delivery (No & %)	14(14.00%)
Indication of CS	Urgent (No & %)	30(34.88%)
	Elective (No & %)	56(65.12%)

Qualitative assay of neonatal outcome measures as regards Apgar score at 5 minutes, 82 cases (82%) ≥ 7 and 12 cases (12%) < 7 , As regard umbilical cord pH was 67% of patients had umbilical cord

pH ≥ 7.2 while 33% of the patients had umbilical cord PH < 7.2 , As Neonatal intensive care unit admission 66% not admitted, while 34% of neonate were admitted to the NICU (**Table 2**).

Table (2): Incidence of low (< 7) Apgar score at 5 minutes, low (< 7.2) UA pH, and ICU admission in the study population

Variables		N	%
Apgar score at 5 min	Normal (≥ 7)	82	82.0%
	Low (< 7)	18	18.0%
UA pH	Normal (≥ 7.2)	67	67.0%
	Low (< 7.2)	33	33.0%
NICU admission	No NICU admission	66	66.0%
	NICU admission	34	34.0%

There was positive correlation between CPR ratio and low Apgar score at 5 min, The MCA/UA PI ratio had poor predictive

value of the low UA PH as p value =0.318 that not statically significant (**Table 3**).

Table (3): Validity of CPR as predictor of Apgar score at 5 minute and measured parameters of umbilical artery pH

Parameters		CPR		Normal (≥ 1.0)		Low (< 1.0)		Total		Chi-Square	
		No	%	No	%	No	%	X ²	P-value		
Apgar score at 5 minute	Normal (≥ 7)	74	88.10	8	50.00	82	82.00	13.215	<0.001*		
	Low (< 7)	10	11.90	8	50.00	18	18.00				
	Total	84	100	16	100.00	100	100.00				
Umbilical artery pH	Normal (≥ 7.2)	58	69.05	9	56.25	67	67.00	0.996	0.318		
	Low (< 7.2)	26	30.95	7	43.75	33	33.00				
	Total	84	100.00	16	100.00	100	100.00				

DISCUSSION

In our study, we found that the mean \pm SD of age was 28.620 \pm 4.273 years, gestational age was 36.240 \pm 1.664 weeks. We found that 34% of neonates were admitted to NICU, as regards Apgar score at 5 min 18(18%) neonates were less than 7, 33(33%) regarding neonatal acidemia of pH less than 7.2.

We found the MCA/UA PI ratio had 62.5% sensitivity and 71.43% specificity as predictors of NICU admission, with cut off value 29.41 positive predictive values and negative predictive value 90.91.

The study showed that the group of MCA/UA PI ratio < 1 was significantly associated with 5 minute Apgar score < 7 8(50%), PH of umbilical artery < 7.2 7(43%), and higher rate of neonatal ICU 10(62.5%).

The result of the current study agreed with *Varsha et al. (2013)* in their prospective observational study that included 100 women with preeclampsia and gestational hypertension who studied the value of cerebro-umbilical pulsatility index ratio in prediction of neonatal outcomes (birth weight, perinatal death, APGAR score at 5 minute, respiratory problems, acidemia and seizure) the

middle cerebral artery /umbilical artery PI had a good specificity of 84.8% and negative predictive value of 90.5%, in ruling out poor Apgar score. In overall prediction of adverse perinatal outcomes, specificity was 87.5% and negative predictive value was 75.5%, indicating that if CPR is normal > 1.08 the likelihood of adverse perinatal outcomes is less.

El-Sokkary et al. (2011) agreed with the current study in their prospective case control study that included one hundred women. They found that the rate of NICU admission and Apgar score < 7 were higher with MCA/UA PI Ratio < 1 . They found that MCA PI/UA PI ratio showed a 73.7% sensitivity and 68.3% specificity and a 52% positive predictive value and 85% negative predictive value in prediction of prenatal outcome (Apgar score < 7) were higher with MCA PI /UA PI < 1 . They found that MCA/UA RI ratio show a higher sensitivity and diagnostic accuracy show 80.6% sensitivity and 69.5% specificity in prediction NICU admission when compared with MCA/UA PI ratio and this is in accordance with the current study where MCA/UA PI ratio show 62.5% sensitivity and 71.43% specificity.

The current study showed poor correlation between MCA/UA PI ratio less than 1 and umbilical PH <7.2 with p value 0.396 (low diagnostic accuracy). MCA/UA PI ratio showed 43.75% sensitivity and 69.05% specificity and a 21.21% PPV and 86.57% NPV in prediction of umbilical pH <7.2.

Regan et al. (2015) suggested an association between CPR and the subsequent development of severe preeclampsia an abnormal CPR is associated with earlier gestational age at delivery and higher rates of neonatal morbidity as compared with those with normal UA Doppler or those with an abnormal UA Doppler, but normal CPR.

We found poor correlation between MCA/UA PI ratio and cord pH as correlation coefficient =1.469, p value =0.318, while *Saber et al. (2019)* found preeclamptic pregnancies with MCA/UA RI <1 carried relative risk of 1.4 (95% confidence interval, 1.2_1.7) of neonatal acidemia (pH <7.2).

Rehana et al. (2016) found MCA/UA PI ratio had 90.91% sensitivity and 78.04% specificity to detect fetus at risk of acidemia, with 52.63% positive and 96.97% negative predictive values.

There was a positive correlation MCA/UA PI ratio and NICU admission, they found MCA/UA PI ratio had 75% sensitivity and 82.92% specificity, with 63.15% positive and 89.47% negative predictive values to detect NICU admission and for the detection of the fetal distress the values were 90.91% sensitivity, 78.04% specificity, 52.63% positive and 96.97% negative predictive values.

In our study, we found MCA/UA PI ratio <1 had excellent correlation predictive value for prediction of the incidence of neonatal ICU admission as evidence by 95% of CI (0.668-8.429), with 62.5% sensitivity, 71.43% specificity estimated positive predictive value =, 29.41% and negative predictive value = 90.91%.

Akolekar et al. (2015) reported that the prediction of adverse outcome by low CPR was better if the time interval between assessment and delivery was < less than or = 2 weeks rather than > 2 weeks and, consequently, suggested that the performance of screening by CPR at 36 weeks may be superior to that at 32 weeks.

We found there was a positive correlation between MCA/UA PI < 1 with Apgar score at 5 min. This agreed with *Allam et al. (2015)*, found that sensitivity and positive predictive values of UA Doppler indices alone were 30 and 50 percent respectively in prediction of poor neonatal outcome. Also they found that sensitivity and PPV of MCA Doppler indices alone were 50 and 46.7 percent respectively. *Asma et al. (2015)* agreed with the current study when Doppler CPR was significantly lower in pregnancy requiring operative delivery or admission the NICU for presumed fetal compromise. UA PI was significantly higher, while MCA PI and CPR were significantly lower, in pregnancies where the newborn was admitted to the NNU. The overall neonatal admission rate in the study cohort was 3.9%.

This study showed that lower fetal CPR was associated with the need for operative delivery for presumed fetal

compromise and with NNU admission at term.

CONCLUSION

MCA PI/UA PI ratio was found to be more sensitive and more specific in prediction of poor neonatal outcome in patients with severe preeclampsia especially in prediction of Apgar score at 5 minutes and incidence of NICU admission.

There was a positive correlation between MCA/UA PI ratio and NICU admission. Doppler data combining both umbilical and cerebral velocimetry provide information on consequences of the placental abnormality; hence Doppler can be a useful tool in the management of patients with preeclampsia and can help in deciding the time of delivery so that the fetus can be saved.

Conflicts of interest: no conflicts of interest were encountered.

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نسبة مقاومة مؤشر الشريان المخى الأوسط للشريان السرى كمعيار لنتائج المواليد لدى الحالات التى تعاني من ارتفاع ضغط الدم المصاحب للحمل

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خلفية البحث: ارتفاع الضغط اثناء الحمل هو مرض متعدد الأنظمة يؤثر على حوالى (5-15%) من مجموع النساء الحوامل، ويعد المسئول الأكبر عن حدوث المضاعفات والوفيات لكل من الأمهات والأجنه قبل واثناء وبعد فترة الولادة. ويتميز هذا المرض بحدوث ارتفاع فى ضغط الدم بشكل مفاجئ وزيادة معدل البروتين فى البول وذلك بعد الأسبوع العشرين من الحمل.

الهدف من البحث: تقييم دور الشريان الدماغى الأوسط ونسبة النبض فى الشريان السرى فى التنبؤ بنتيجة الأطفال حديثي الولادة فى الحمل الناجم عن ارتفاع ضغط الدم.

المريضات وطرق البحث: شملت هذه الدراسة 100 امرأة مصابة بإرتفاع ضغط الدم المصاحب للحمل والتي تم إجرائها فى مستشفى السيد جلال الجامعى من نوفمبر 2018 إلى يوليو 2019 إلى تقييم نسبة المعامل النبضى للشريان الدماغى الأوسط إلى الشريان السرى فى التنبؤ بنسبة دخول حديثي الولادة إلى وحدة الاطفال المبتسرين و فترة العلاج ومعدل أبحار المنخفض بعد 5 دقائق من الولادة فى الأمهات اللاتى تعانين من إرتفاع ضغط الدم المصاحب للحمل.

نتائج البحث: وقد وجدنا أن أفضل قيمة مستقلة لنسبة المعامل النبضى للشريان المخى الأوسط إلى الشريان السرى فى التنبؤ بمعدل دخول الأطفال حديثي الولادة إلى وحدة الاطفال المبتسرين، وهي أفضل قيمة مستقلة لنسبة المعامل النبضى للشريان الدماغى الأوسط إلى الشريان السرى هي (62.5%) من الحساسيه، (71.43% على وجه التحديد). و دل هذا عن نسبة مؤشر المعامل النبضى للشريان الدماغى الأوسط او الشريان السرى بشكل مستقل. وكانت نسبة المعامل النبضى للشريان المخى الأوسط الى الشريان السرى كانت منبئاً جيداً على توقع النتيجة

الضعيفة للطفل حديث الولادة عند المرضى الذين يعانون من ارتفاع ضغط الدم الناجم عن الحمل خاصة في التنبؤ بدخول الأطفال حديثي الولادة إلى وحدة الاطفال المبتسرين.

الإستنتاج: توفر بيانات دوبلر التي تجمع بين كل من قياس السرعة السريري والدماعي معلومات عن عواقب تشوهات المشيمة. وبالتالي؛ يمكن أن يكون الدوبلر أداة مفيدة في إدارة المرضى الذين يعانون من تسمم الحمل ويمكن أن يساعد في تحديد وقت الولادة بحيث يمكن الحفاظ علي الجنين.