

Role Of Middle Cerebral Artery / Umbilical Artery Pulsatility Index Ratio (cerebro-placental ratio CPR) For Prediction Of Fetal Outcome In Preeclamptic Patients

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Abstract

Objective: The aim of this prospective observational study is to assess the accuracy of Doppler indices of umbilical and middle cerebral especially fetal middle cerebral artery/umbilical artery pulsatility index ratio during third trimester in predicting acidemia and low Apgar score at 5 minutes after birth in neonates of women with preeclampsia. To provide basis for use of Doppler tests in directing treatment protocol for preeclamptic patients.

Methods :Studydesign:Cohort observational study among women with preeclampsia.

Studysetting: One hundred cases who were at 32 to 40 weeks of gestation with preeclampsia(from March 2017 to March 2018) attended antenatal clinic and emergency room at obstetrics and gynecology department, faculty of medicine, Sohag University Hospital. Ultrasound was performed at fetal care unit at Sohag University Hospital.

Results : This observational cross-sectional study was designed to assess Doppler indices of umbilical artery as predictor of neonatal outcome among women with preeclampsia.A total 100 pregnant women with preeclampsia were recruited in the study

Conclusion : We recommend adding MCA (PI)/ UA (PI) ratio to routine antepartum fetal surveillance from 32 weeks gestations for women with preeclampsia as there is a strong correlations between it and poor neonatal outcome.

Keywords :Preeclampsia, umbilical artery,middle cerebral artery, Neonatal outcome.

Introduction

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. The incidence of various hypertensive disorder of pregnancy varies widely from 5 to 15% throughout the globe.It accounts for a total of 7-10% of perinatal mortality in developed countries and 20% in developing countries. The perinatal mortality is 5% in mild PIH and 15 to 25% in severe PIH (*Smitha et al., 2014*).There are four major hypertensive disorders that occur in

pregnant women according to (*American College of Obstetricians and Gynecologists, 2013*):Preeclampsia-eclampsia ,Chronic (preexisting hypertension ,Preeclampsia-eclampsia superimposed upon chronic hypertension and Gestational hypertension. Preeclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks' gestation and can present as late as 4-6 weeks postpartum. It is clinically defined by hypertension and proteinuria, with or without pathologic edema (*Lagna et*

al., 2015). Preeclampsia is defined as the presence of a systolic blood pressure (SBP) greater than or equal to 140 mm Hg or a diastolic blood pressure (DBP) greater than or equal to 90 mm Hg or higher, on two occasions at least 4 hours apart in a previously normotensive patient (*Lagna et al., 2015*). In addition to the blood pressure criteria, proteinuria of greater than or equal to 0.3 grams in a 24-hour urine specimen, a protein (mg/dL)/creatinine (mg/dL) ratio of 0.3 or higher, or a urine dipstick protein of 1+ (if a quantitative measurement is unavailable) is required to diagnose preeclampsia (*Lagna et al., 2015*). Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring (*Dubiel et al., 2000*). 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 (*Hernandez-Andrade et al., 2004*).

Patients and

Methods: Study design: Cohort observational cross-sectional study among women with preeclampsia. **Study setting:** One hundred cases who were at 32 to 40 weeks of gestation with preeclampsia (from March 2017 to March 2018) attended antenatal clinic and emergency room at obstetrics and gynecology department, faculty of medicine, Sohag University Maternity Hospital

Participant: Inclusion criteria: Age (20-35) years old, Gestational age more than 32 weeks that was confirmed, either by menstrual dates or by first trimester ultrasonography, Singleton intrauterine pregnancy, Living fetus, Preeclampsia diagnosed as new onset hypertension (Systolic blood pressure of 140 mm Hg or higher, or

diastolic blood pressure of 90 mmHg or higher, on two occasions at least 6 Hours apart while the patient is on bed rest unless antihypertensive therapy is initiated before this time) and Proteinuria (>300mg/24h) (*American College of Obstetricians and Gynecologists, 2013*). **Exclusion criteria:** Women with multiple pregnancies, A history of chronic hypertension, Diabetes mellitus, Autoimmune diseases, Intrauterine fetal death on admission, Congenital abnormalities of the fetus, The pregnant woman in labour, HELLP syndrome, Impending eclampsia. **Sample size justification:** Sample size has been calculated using PASS[®] version 11 program (*Hintze, 2011*). 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. **Sampling plan:** Systemic random sample was used for selection of cases. **Methodology:** All women were subjected to: **Complete history to exclude any preexisting maternal disease or pregnancy complication:** Personal history: including name, age, occupation, marital status, residency and special habits of medical important, Present history: including calculation of the gestational age in weeks, any complaints during pregnancy, the warning symptoms and all investigations she had done in that pregnancy, Menstrual history: including LMP, Obstetric history, Contraceptive history, Past history for the presence of any medical disorders, Family history for any medical disorders in the family

especially hypertension, **General examination:** Blood pressure was measured in a semi-recumbent positions with the head and chest slightly elevated using standard mercury sphygmomanometer. Two blood pressure recordings 6 hours apart as recommended by the American College of Obstetricians and Gynecologists. Chest and heart examination. Edema was tested for pitting in the lower limbs, ankles and shin of the tibia, checking for edema of the lower abdomen and testing for ascites. **Abdominal examination:** for edema and loin exam. **Laboratory investigations:** complete blood picture, complete urine analysis, random blood glucose, liver function test, renal profile, blood coagulation profile,

prothrombintime. **Ultrasonography:** for number of fetuses, presence of fetal heart activity, fetal biometry, presence of any apparent congenital anomalies, amount of liquor and placental site. The four standard biometric parameters commonly used to estimate gestational age and/or fetal weight in the second and third trimesters are: biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) (*Hadlock, 1991*).

Intervention: Doppler studies among preeclamptic women done to measure the middle cerebral artery and umbilical artery Doppler indices especially pulsatility index and values below the 5th percentile were considered as abnormal. 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. All sonographic examinations were performed trans-abdominally using a GE Voluson S6

ultrasound machine at the tertiary care center at Sohag Hospital.

Mode of delivery: Vaginal delivery if CPR is more than 1 (Induction of labor or Spontaneous vaginal delivery) or Cesarean section if CPR is less than 1 (Elective C.S. or Urgent C.S.)

Fetal outcomes: The neonates were observed for major and minor adverse outcomes.

Major adverse outcomes: Perinatal deaths, hypoxic ischemic encephalopathy, intraventricular hemorrhage, sepsis and necrotizing enterocolitis.

Minor adverse outcomes: Caesarean delivery for fetal distress, fetal asphyxia, low birth weight and preterm delivery.

Neonatal assessment by APGAR score. A useful clinical tool to identify those neonates who require resuscitation as well as to assess the effectiveness of any resuscitative measures is the Apgar scoring system (*Cunningham et al., 2005*), each of the five easily identifiable characteristics heart rate, respiratory effort, muscle tone, reflex irritability, and color is assessed and assigned a value of 0 to 2. The total score, based on the sum of the five components, is determined 5 minutes after delivery. The 5 minute score, is a useful index of the effectiveness of resuscitative efforts. The 5 minute Apgar score also has prognostic significance for neonatal survival is related closely to the condition of the infant in the delivery room (*Cunningham et al., 2005*). According to the study done in the emergency room on 100 pregnant women who are at 32 to 40 weeks of gestation with preeclampsia, the majority of them were admitted to the labor theater and delivery room were they spent few days till delivery. A minor portion of those cases were admitted for immediate delivery. fetal blood pH measurement was done within 5 minutes of delivery. Apgar score was determined at 1 minute and 5 minutes

after birth Neonatal morbidity was established if Apgar score <7 at 5 minutes. Neonatal acidemia of pH<7.2. Newborn was admitted to the neonatal intensive care unit (NICU). **Statistical analysis:** The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 20 for windows; SPSS Inc, Chicago, IL, 2001). Quantitative variables are expressed as mean and

SD or as median and interquartile range (IQR) in cases of non-parametric variables. Qualitative variables was expressed as frequencies and percent. **Student t test** and **Mann Whitney Test** were used to compare a continuous variable between two study groups. **Chi square** and **Fisher's exact tests** were used to examine the relationship between Categorical variables. P-value <0.05 was considered statistically significant.

Result

Age (years)	Range	20-35
	Mean ±SD	28.6±4.2
Gestational age (weeks)	Range	32-40
	Mean ±SD	34.2±1.6
Body mass index(kg/m2)	Mean ±SD	24.1±1.4
Parity	P0	22(22.00%)
	P1	28(28.00%)
	P2	28(28.00%)
	P3	20(20.00%)
	P4	2(2.00%)

Table (1): Characteristics of the study population

UA_PI	Range	0.4-1.9
	Mean ±SD	0.8±0.2
UA_RI	Range	0.3-1.8
	Mean ±SD	0.7±0.1
UA_S/D ratio	Range	1.6-4.1
	Mean ±SD	3.1±1.3

Table (2): Doppler indices of Umbilical Artery in the study population

PI Pulsatility index

RI Resistance index

S/D ratio Systolic/Diastolic ratio

MCA_PI	Range	0.5-2.67
	Mean ±SD	1.2±0.5
MCA_RI	Range	0.4-1.7
	Mean ±SD	0.7±0.1
MCA_S/D ratio	Range	1.4-7.8
	Mean ±SD	5.4±2.7

Table (3): Doppler indices of Middle Cerebral Artery in the study population

PI Pulsatility index

RI Resistance index

S/D ratio Systolic/Diastolic ratio

MCA_PI	Range	0.5-2.6
	Mean ±SD	1.2±0.5
UA_PI	Range	0.4-1.9
	Mean ±SD	0.8±0.2
CPR	Range	0.6-3.1
	Mean ±SD	1.6±0.6
CPR	Normal (more than 1)	84(84.00%)
	Low (less than 1)	16(16.00%)

Table (4): Cerebro-placental Ratio (CPR) in the study population
CPR Cerebroplacental Ratio

UA-PI	CPR		T-Test	
	Normal (1.0)	Low (<1.0)	t	P-value
Range	0.4-1.91	0.7-1.5	-2.797	0.006*
Mean ±SD	0.767±0.278	0.978±0.259		

Table (5): The correlation between Doppler ultrasound indices in included women and the CPR.

	Correlations	
	CPR	
	r	P-value
Age	0.078	0.501
SBP	-0.132	0.326
DBP	-0.166	0.131
MAP	-0.147	0.145
GA	0.303	0.053*
UA_PI	-0.336	0.001*
Apgar	0.231	0.021*
PH	0.086	0.396

Table (6):The correlation between CPR and patients characteristics and Doppler indices

Discussion

Ebrashy et al. (2005) in their prospective case control study that included 50 pregnant women with preeclampsia, they found preeclamptic pregnancies with MCA/UA RI<1 carried relative risk of 1.4(95% confidence interval, 1.2_1.7) of neonatal academia (pH <7.2). **Shahinaj et al. (2010)** in their prospective observational study that included 738 patients with

preeclampsia. It was found that in the group of abnormal MCA/UA PI there were a significant higher rates of

NICU admission 202(77.6%), Apgar scores less than 7 at 5 minute 161(61.9%). MCA/UA PI ratio had 50.1% sensitivity and 79.3% specificity to detect need for NICU admission, with 77.6% positive and 52.5% negative predictive values. The value for prediction of the incidence of NICU admission as evidenced by area under the curve was 0.714 with 95% CI (0.609 to 0.819), the best cut off value was 0.8, this cutoff value with 100% sensitivity, 97.96% specificity, estimated positive predictive 75% and negative value 100%. **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 ($p < 0.05$). 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 ($p < 0.05$). **Alkolekar et al. (2015)**, in their prospective case control study that included 6178 pregnant women in routine screening for adverse neonatal outcome at 35-37 weeks' gestation, their study 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. They found that the CPR provided poor prediction of indicators for adverse perinatal outcome and it is therefore unlikely that such assessment would improve perinatal outcome. But showed that the measurement of CPR can contribute in the differentiation of constitutionally small from growth restricted fetuses. The strengths of this study are firstly, prospective examination of a large population of pregnant women attending for routine care in the 3rd trimester of pregnancy, secondly, application of multivariable regression analysis to define the contribution and interrelations of variables that influence the measured values of MCA_PI and UA_PI. The main limitation of the study is that the data were confined to the third trimester of pregnancy. **Conclusion and Recommendations:** We recommend adding MCA (PI)/ UA (PI) ratio to routine antepartum fetal surveillance from 32 weeks gestations for women with preeclampsia as there is a strong

correlations between it and poor neonatal outcome.

References

1. **Akolekar R, Sarno L, Wright A, Wright D and Nicolaides KH.:** Fetal middle cerebral artery and umbilical artery pulsatility index: effects of maternal characteristics and medical history. *Ultrasound ObstetGynecol*, 2015; 45: 402-408.
2. **Alaam NE and Maarouf TM.:** Cerebroplacental Doppler indices ratio and perinatal outcome among high risk pregnancy. *Journal of American science*, 2015; 11(6): p: 170-174.
3. **Asma AK, Morales-Rosello J, Morlando M, Hannan H, Bhide A, Papageorgiou A, Thilaganathan B.:** Is fetal cerebroplacental ratio an independent predictor of intrapartum fetal compromise and neonatal unit admission? *American J of Obst and Gyne*, 2015; P1-10.
4. **Dewbury KC, Meire HB, Cosgrove DO and Farrant P.** Doppler in obstetrics. In: *clinical ultrasound: a comprehensive text-ultrasound in obstetrics and gynecology*. Dewbury KC, Meire HB, Cosgrove DO and Farrant P (eds). 2nd ed. Churchill, Livingstone, London, 2001; 259-277.
5. **Ebrashy A, Azmy O, Ibrahim M, Waly M.:** Middle cerebral/umbilical artery resistance index ratio as sensitive parameter for fetal well-being and neonatal outcome in patients with preeclampsia: case-control study. *Croat J Med J*, 2005; 46(5): 826-831.
6. **El-Sokkary M, Omran M and Ahmed H.:** Ratio of middle cerebral artery umbilical artery Doppler velocimetry and status of newborn in post-term pregnancy. *Br Med J*, 2011; 280: 282-283.