Cerebroplacental Ratio and Cerebrouterine Ratio in Predicting Neonatal Outcome in Preeclamptic Pregnant Women - ⊗

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ABSTRACT

**Background:** Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become an established method of antenatal monitoring. Cerebroplacental and Cerebrouterine ratios have been studied to predict neonatal outcomes.

**Aim of the Work:** To assess if Cerebrouterine Ratio would be complementary to cerebroplacental Ratio in predicting adverse neonatal outcome in preeclamptic pregnant women.

**Patients and Methods:** The current study was carried out at Ain Shams University Maternity Hospital on (250) pregnant women with singleton pregnancies who were admitted to the Ain shams maternity Hospital presented with preeclampsia 34-37 weeks gestation, during a period from July 2017 to March 2018.

**Results:** The current study showed that among patients with abnormal CP ratio 35 case (47%) had fetal distress, 13 case (17.6%) were small for gestational age, 55 cases (47.3%) had APGAR 1 min < 7, 44 cases (59.5%) had APGAR 5 min < 7, 57 case (77%) admitted to NICU, and 9 cases (12.2%) suffered from Neonatal death, while among patient with abnormal CU ratio 49 case (45.8%) had fetal distress, 14 case (13.1%) were small for gestational age, 73 cases (68.2%) had APGAR 1 min < 7, 59 cases (55.1%) had APGAR 5min < 7, 79 case (73.8%) admitted to NICU, and 15 cases (14%) suffered from Neonatal death. In our study, Abnormal CP ratio and CU ratio are related to unfavorable pregnancy outcome. CU ratio had higher sensitivity and negative predictive value than CP ratio in prediction of APGAR 5 min, foetuses small for gestational age, foetal distress, NICU admission and neonatal death. Combining both ratios improved the specificity and prediction characteristics of neonatal outcomes compared to any of the ratios used alone.

**Conclusion:** Cerebrouterine ratio and cerebroplacental ratio were complementary to each other in predicting the adverse neonatal outcomes, than any of the ratios alone.

**Recommendations:** Cerebrouterine and cerebroplacental ratios should to be used complimentary to each other to predict neonatal outcome in cases of preeclampsia. The value of CP and CU ratios in smaller gestational ages should be investigated to predict neonatal outcome.

**Keywords:** Cerebroplacental ratio; Cerebrouterine ratio; Neonatal outcome; Preeclampsia

INTRODUCTION

Pre-eclampsia, one of the leading causes of maternal and fetal morbidity and mortality, affecting 2-5% of pregnancies, is a specific syndrome characterized by reduced organ perfusion secondary to vasospasm and endothelial pathophysiology [1].

Preeclampsia contributes greatly to IUGR (Intra Uterine Growth Restriction), preterm labor through affecting development of uteroplacental and fetoplacental circulation necessary for a normal pregnancy outcome [2].

Doppler velocimetry of multiple feto-placental vessels is a non-invasive technique that evaluates abnormal fetal hemodynamics that take place in response to changes in placental resistance [3], can be used to monitor compromised fetus predicting adverse perinatal outcome and assisting in optimal time of delivery [4].

Umbilical artery and middle cerebral artery Doppler ultrasound clearly depict the information about placental resistance and the changes in the fetal hemodynamics in response to it. Umbilical artery Doppler reflects the maldevelopment of the placental tertiary stem villi which increases the placental resistance [1].

Fetal Middle Cerebral Artery (MCA) resistance in combination with Umbilical Artery (UA) resistance as the Cerebroplacental Ratio (CPR) is more reflective of fetal hypoxia and acidemia, and therefore better prediction of perinatal outcome which also aid in the prediction of both SGA and adverse perinatal outcome [5].

Uterine artery Doppler might be expected to reflect placental perfusion, while umbilical Doppler reflects placental pathology, therefore The Cerebrouterine Ratio (CU Ratio) could have a better predictive value for adverse outcome [6].

The aim of the study is to assess if CU ratio is complementary to CP ratio in prediction of neonatal outcome.

METHODOLOGY

This study for accuracy of a diagnostic test was carried out at Ain Shams University Maternity Hospital on (250) pregnant women with singleton pregnancies who were admitted to the Ain Shams maternity Hospital presented with preeclampsia 34-37 weeks gestation, during a period from July 2017 to March 2018, patients with DM, fetal congenital anomalies, IUGR and Rh incompatibility were excluded .

After taking informed written consent the recruited patients were subjected to detailed history taking and examination, routine lab tests as CBC, liver and kidney function tests were performed as well as urine dipstick for protein assessment.

Ultra-sonographic scanning was done trans-abdominally using Medison R5 Ultrasound machine equipped with a 3.5 MHz Convex probe to evaluate fetal weight, biometry and doppler studies. Umbilical Artery (Um.A), Middle Cerebral Artery (MCA), Uterine Artery (Ut.A), were examined by Color Doppler ultrasound and Pulsed wave Doppler.

**Middle Cerebral Artery (MCA) Doppler technique**

A transverse view of the fetal brain is obtained at the level of the biparietal diameter. The transducer is then moved towards the base of the skull at the level of the lesser wing of the sphenoid bone. Using color flow imaging, the middle cerebral artery can be seen as a major lateral branch of the circle of Willis, running anterolaterally at the borderline between the anterior and the middle cerebral fossae. The pulsed Doppler sample gate is then placed on the middle portion of this vessel to obtain flow velocity waveforms. Using color-flow mapping with low-pass filter was set at 50Hz, the angle of insonation should be minimized and kept < 150. During the studies, care should be taken to apply minimal pressure to the maternal abdomen with the transducer, as fetal head compression is associated with alterations of
intracranial arterial waveforms, Doppler wave forms were obtained, values of PI < 5th percentile is abnormal [7].

**Uterine artery Doppler technique**

Doppler velocity of uterine artery was recorded at the point at which they crossed over the external iliac artery cranial to crossing of iliac artery. Mean of the PI of both uterine arteries was taken, values of PI > 95th percentile is abnormal [8].

**Umbilical artery Doppler technique**

The transducer is placed on the mother’s abdomen overlying the foetus and is systematically manipulated to obtain the characteristic waveforms from the umbilical artery and vein. With a pulsed wave Doppler system, an ultrasound scan is first carried out, a free-floating portion of the cord is identified and the Doppler sample volume is placed over an artery and the vein, parallel to blood flow, using color-flow mapping with low-pass filter was set at 50Hz, the angle of insonation should be minimized and kept between 150 - 60°. Umbilical venous blood flow increases with fetal inspiration (during which the fetal abdominal wall moves inward) and decreases with expiration (during which the wall moves outward). There is also a breathing-related modulation of arterial pulsatility, and umbilical artery Doppler studies should be avoided during fetal breathing. Once waveforms are obtained with a clear envelope, at least three waveforms can be averaged and impedance indices calculated. Values of PI > 95th percentile were considered abnormal [7].

- Cerebroplacental ratio (CP) (middle cerebral artery to umbilical artery PI ratio) was estimated.
  - (CP) ratio is plotted on the chart; < 5th percentile were considered abnormal.
- Cerebrouterine ratio (CU) (middle cerebral artery to uterine artery PI ratio) was estimated.
  - (CU) ratio is plotted on the chart; < 5th percentile were considered abnormal [6].

Outcome variables included are Low APGAR score (5 min APGAR score less than 7), small for gestational age (weight below 10th percentile for gestational age), neonatal death, admission to NICU.

Pregnancy outcome was considered to be Uneventful or Favourable when the above complications were absent. The outcome for each pregnancy was obtained by examining the labour ward records and neonatal intensive care unit records wherever appropriate.

**RESULTS**

The current study is a prospective observational study that was held in Ain Shams university maternity hospital, during the period between July 2017 and March 2018. The aim was to evaluate the predictive value of (CU) ratio complementary to (CP) ratio for prediction of adverse neonatal outcome in patients with Preeclampsia. This study included 250 women with preeclampsia out of which 117 women were severe preeclampsia and 133 women were mild preeclampsia. Concerning the demographic data of patients, the mean age was 29.7 ± 3.5 years, the mean BMI was 25.5 ± 1.4 Kg/m², the mean gestational age was 35.5 ± 0.9 weeks and regarding the parity 34% of the women were PG and 66% were multipara. More than half of the studied cases had MCA-PI and Um-PI abnormalities, less than half of the studied cases had UtA-PI, CP ratio and CU ratio abnormalities. Poor outcomes were significantly more frequent among a cases with abnormal CU ratio and CP ratio.

The current study showed that abnormal CP ratio and CU ratio were significantly more frequent in patients with severe preeclampsia.

**DIAGNOSTIC CHARACTERISTICS OF CP AND CU**

Table 1 shows that CU ratio had higher sensitivity & NPV and lower specificity & PPV than CP ratio in prediction of fetal distress. Combining the CP ratio and CU ratio findings improved the specificity and PPV than either ratio alone.

Table 2 shows that CU ratio had higher sensitivity and lower specificity & PPV than CP ratio in prediction of small for GA delivery. Combining the CP and CU findings improved the specificity and diagnostic accuracy than either ratio alone.

CU ratio had higher sensitivity & NPV and lower specificity & PPV than CP ratio in prediction of APGAR 1 min < 7. Combining the CP and CU findings improved the specificity and PPV than either ratio alone.

<table>
<thead>
<tr>
<th>Characters</th>
<th>Value</th>
<th>95% CI</th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>42.4%</td>
<td>28.5%-56.3%</td>
<td>57.6%</td>
<td>46.6%-68.4%</td>
</tr>
<tr>
<td>Specificity</td>
<td>74.3%</td>
<td>35.6%-59.3%</td>
<td>45.8%</td>
<td>36.1%-55.7%</td>
</tr>
<tr>
<td>PPV</td>
<td>88.1%</td>
<td>82.3%-92.5%</td>
<td>95.1%</td>
<td>90.2%-96.0%</td>
</tr>
<tr>
<td>NPV</td>
<td>73.4%</td>
<td>67.1%-79.0%</td>
<td>59.4%</td>
<td>52.7%-65.8%</td>
</tr>
<tr>
<td>DA</td>
<td>63.6%</td>
<td>57.3%-69.6%</td>
<td>54.4%</td>
<td>48.0%-60.7%</td>
</tr>
</tbody>
</table>

Table 2: Diagnostic characteristics of CP and CU ratios in prediction of small for GA.

<table>
<thead>
<tr>
<th>Characters</th>
<th>Value</th>
<th>95% CI</th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>81.0%</td>
<td>58.1%-94.6%</td>
<td>47.6%</td>
<td>25.7%-70.2%</td>
</tr>
<tr>
<td>Specificity</td>
<td>58.1%</td>
<td>51.4%-64.5%</td>
<td>74.7%</td>
<td>68.5%-80.2%</td>
</tr>
<tr>
<td>PPV</td>
<td>60.0%</td>
<td>53.6%-66.1%</td>
<td>72.4%</td>
<td>66.4%-77.8%</td>
</tr>
<tr>
<td>NPV</td>
<td>39.0%</td>
<td>21.1%-57.0%</td>
<td>22.3%</td>
<td>0.2%-44.4%</td>
</tr>
<tr>
<td>DA</td>
<td>15.0%</td>
<td>9.0%-23.0%</td>
<td>14.7%</td>
<td>7.3%-25.4%</td>
</tr>
<tr>
<td>NPV</td>
<td>97.1%</td>
<td>92.7%-99.2%</td>
<td>94.0%</td>
<td>89.4%-96.9%</td>
</tr>
</tbody>
</table>

DISCUSSION

Simanaviciute and Gudmundsson [6] showed that abnormal CU ratio was significantly more frequent in patients with severe preeclampsia, while the results obtained by Eser et al. [9] showed that abnormal CU ratio was more frequent in patients with mild preeclampsia.

The current study showed that among patients with abnormal CP ratio 35 cases (47%) had fetal distress, 13 cases (17.6%) were small for gestational age, 55 cases (47.3%) had APGAR 1 min < 7, 44 cases (59.5%) had APGAR 5 min < 7, 57 cases (77%) admitted to NICU, and 9 cases (12.2%) suffered from Neonatal death, while among patients with abnormal CU ratio 49 cases (45.8%) had fetal distress, 14 cases (13.1%) were small for gestational age, 73 cases (68.2%) had APGAR 1 min < 7, 59 cases (55.1%) had APGAR 5 min < 7, 79 cases (73.8%) admitted to NICU, and 15 cases (14%) suffered from Neonatal death, This shows that abnormal CP ratio and CU ratio are related to unfavorable pregnancy outcome.

This is consistent with the results obtained by Adiga et al. [10], in their prospective observational study that included 100 women with “hypertension peculiar to pregnancy” (preeclampsia and gestational hypertension) who studied the value of CP ratio and CU ratio in prediction of neonatal outcomes, both had good negative predictive value in predicting adverse neonatal outcome.

This also agreed with the results obtained by Smitha et al. [2], Simanaviciute and Gudmundsson [6] and Eser et al. [9].

The current study showed that CP ratio had 50% sensitivity, 81.5% specificity, 70.4% Diagnostic accuracy, 59.5% positive predictive value and 75% negative predictive value to predict newborns with APgar 5 min < 7, with statistically significant positive correlation as correlation coefficient = 2.7, p value < 0.001.

Also Adiga et al. [10] showed significant positive correlation between abnormal CP ratio and APGAR 5 min < 7. The results showed that CP ratio had 56.3% sensitivity, 84.8% specificity and 80% Diagnostic accuracy, 42.9% positive predictive value and 90.5% negative predictive value to predict newborns with Apgar 5 min < 7., also the result obtained by Smitha et al. [2] and Fong et al. [11] showed significant positive correlation between abnormal CP ratio and APGAR 5 min < 7.

On the other hand Eser et al. [9], in their cross sectional study that included 185 women, that studied the predictive value of CP ratio and CU ratio in prediction of neonatal outcomes in preeclampsia. showed no significant positive correlation between abnormal CP ratio and poor Apgar score, as P = 0.1, showed no significant positive correlation between abnormal CP ratio and poor Apgar score, as P...
value = 0.1. The results showed that CP ratio had 42.8% sensitivity and 74.3% specificity, 9.7% positive predictive value and 94.1% negative predictive value, 9.7% positive predictive value and 94.1% negative predictive value to predict newborns with Apgar 5 min < 7.

In the present study CU ratio had 67% sensitivity, 70.4% specificity, 69.2% Diagnostic accuracy, 55.1% positive predictive value and 79.7% negative predictive value to predict newborns with Apgar 5 min < 7 with positive predictive value 55.1% and negative predictive value 79.7%, to predict newborns with Apgar 5 min < 7, with statistically significant positive correlation as correlation coefficient = 2.3, p value < 0.001.

Also Adiga et al. [10] showed significant positive correlation between abnormal CU ratio and Apgar 5 min < 7, as P value = 0.044, the result showed that CU ratio had 62.5% sensitivity and 64.6% specificity, 64.2% Diagnostic accuracy, 26.2% positive predictive value and 89.5% negative predictive value to predict newborns with Apgar 5 min < 7. The result obtained by Smitha et al. [2] and Fong et al. [11] show significant positive correlation between abnormal CU ratio and Apgar 5 min < 7.

On the other hand Eser et al. [9] showed no significant positive correlation between abnormal CU ratio and poor Apgar score, as P value = 0.4, the results showed that CU ratio had 27.2% sensitivity and 57.9%, 3.8% positive predictive value and 89.8% negative predictive value to predict newborns with Apgar 5 min < 7, also Simanaviciute and Gudmundsson [6] showed no significant correlation.

In the present study CP ratio had 61.9% sensitivity, 73.4% specificity and 72.4% Diagnostic accuracy, 17.6% positive predictive value and 95.5% negative predictive value to detect fetuses small for GA, while CU ratio had 66.7% sensitivity, 59.4% specificity and 60% Diagnostic accuracy, 13.1% positive predictive value and 95.1% negative predictive value to detect fetuses small for GA, with statistically significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses small for GA, as correlation coefficient: 2.3, p value < 0.001, correlation coefficient = 1.6, p value = 0.021, respectively.

Adiga et al. [10] showed significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses small for GA, the result showed that CP ratio had 33.3% sensitivity, 83.9% specificity, 66.3% Diagnostic accuracy, 52.4% positive predictive value and 70.3% negative predictive value, to detect fetuses small for GA while CU ratio had 54.5% sensitivity, 67.7% specificity and 63.2% Diagnostic accuracy, 47.77% positive predictive value and 63.2% negative predictive value, to detect fetuses small for GA, also Simanaviciute and Gudmundsson [6] show significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses small for GA.

On the other hand Eser et al. [9], found no significant correlation between abnormal CP and abnormal CU ratio with fetuses small for GA, as P value = 0.07 P value = 0.08 respectively, the result showed that CP ratio had 31.1% sensitivity and 75.4% specificity, 36.2% positive predictive value and 70.4% negative predictive value to detect fetuses small for GA, while CU ratio had 47.8% sensitivity and 63.9% specificity, 38%positive predictive value and 72.9% negative predictive value to detect fetuses small for GA.

In the present study CP ratio had 41.6 % sensitivity, 85 % specificity, 61.2 % Diagnostic accuracy, 77% positive predictive value and 54.5% negative predictive value to predict need for NICU admission while CU ratio had 57.7% sensitivity, 75.2% specificity, 65.6% Diagnostic accuracy, 73.8% positive predictive value and 59.4% negative predictive value to predict need for NICU admission, these results showed statically significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses with NICU admission, as correlation coefficient = 2.8, p value < 0.001, correlation coefficient = 2.3, p value < 0.001, respectively.

These results agreed with the results obtained by Eser et al. [9], that show significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses with NICU admission, as P value = 0.0006, P value = 0.0009, respectively, also Smitha et al. [2] showed significant positive correlation as P value < 0.001.

On the other hand Simanaviciute and Gudmundsson [6] in their cross sectional study that included 231 women, who studied CU ratio in normal and preeclamptic pregnancies and comparing it to CP ratio in predicting an unfavorable outcome of pregnancy, found no significant positive correlation between abnormal CP ratio and abnormal CU ratio with fetuses with NICU admission.

In the present study CP ratio had 45 %sensitivity, 71.7%specificity, 69.6%Diagnostic accuracy, 12.2% positive predictive value and 93.8% negative predictive value to detect Neonatal death, while CU ratio had 75 % sensitivity, 60 % specificity, 61.2 % Diagnostic accuracy, 14 % positive predictive value and 96.5 % negative predictive value to detect Neonatal death, showed no statistically significant correlation between abnormal CP ratio and Neonatal death, as correlation coefficient = 1.6, p value = 0.116.

Shahinaj et al. [12], in their prospective observational study that included 738 singleton pregnancies, that studied The value of the CP ratio in the prediction of neonatal outcome in patient with preeclampsia, found positive correlation and statistically significant between abnormal CP ratio and Neonatal death as P value < 0.0001, the result showed that CP ratio had 97.7 % sensitivity and 66.0 % specificity to predict Neonatal death, with positive predictive value 16.5 % and negative predictive value 99.7%, while CU ratio had 50% sensitivity and 65.8% specificity to detect neonatal death, with positive predictive value 40% and negative predictive value 74.3%.

In the present study CP ratio had 62.5% sensitivity, 79.9% specificity and 76% Diagnostic accuracy to detect Fetal distress, with positive predictive value 47.3% and negative predictive value 88.1%, while CU ratio had 87.5% sensitivity, 70.1% specificity and 74.0% Diagnostic accuracy to detect Fetal distress, with positive predictive value 45.8% and negative predictive value 95.1% with statistically significant positive correlation between abnormal CP ratio and CU ratio with fetuses with Fetal distress, as correlation coefficient = 3.1, P value < 0.001, correlation coefficient = 2.9, P value < 0.001, respectively.

Also, Eser et al. [9] found statically significant positive correlation between abnormal CP and abnormal CU ratio with fetal distress as P value = 0.0008, P value = 0.004, respectively, the results showed that CP ratio had 34.7% sensitivity and 96% specificity to detect Fetal distress, with positive predictive value 96% and negative predictive value 12%, while CU ratio had 55.1% sensitivity and 97% specificity to detect Fetal distress, with positive predictive value 96% and negative predictive value 19.3%.

CU ratio had higher sensitivity and negative predictive value than CP ratio in prediction of APGAR 5 min, foetuses small for gestational age, foetal distress, NICU admission and neonatal death, while CP
ratio had higher specificity and positive predictive value than CU ratio in prediction of APGAR 5 min, foetuses small for gestational age, foetal distress, NICU admission and neonatal death. Combining both ratios improved the specificity and prediction characteristics of neonatal outcomes compared to any of the ratios used alone.

CONCLUSION

Cerebrouterine ratio and cerebroplacental ratio were complementary to each other in predicting the adverse neonatal outcomes, than any of the ratios alone.

RECOMMENDATIONS

Cerebrouterine and cerebroplacental ratios should to be used complimentary to each other to predict neonatal outcome in cases of preeclampsia.

The value of CP and CU ratios in smaller gestational ages should be investigated to predict neonatal outcome.

REFERENCES


