CORRELATION OF CEREBROPLACENTAL RATIO WITH PERINATAL OUTCOME IN INTRAUTERINE GROWTH RESTRICTION
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ABSTRACT

BACKGROUND
Doppler velocimetry is a non-invasive method of measuring changes in blood flow. Randomised Control Trials (RCTs) have shown that using Doppler indices in the management of Intrauterine Growth Restriction (IUGR) cases leads to a significant reduction in perinatal mortality rate. Deterioration of various Doppler indices precedes abnormal Biophysical Profile (BPP) by 1-2 weeks. Umbilical artery indices only reflect the placental status. Fetal response to this increasing placental insufficiency can be deduced from studying the Cerebroplacental Ratio \{CPR\}, which gives us an idea of the fetal response to the placental status and is potentially more advantageous in predicting fetal outcome.

OBJECTIVES
To compare CPR in predicting fetal outcome with UA and MCA indices.

MATERIALS AND METHODS
Prospective cohort study of cases of IUGR - January 2013 to December 2013. 180 cases of clinically diagnosed IUGR were selected. Obstetric USG and Doppler was performed. The S/D ratio, RI, PR values were obtained and CPR calculated. All cases were managed as per the protocol then in place using U/A SD ratios for determining the timing & mode of termination

RESULTS
Of 180 cases of IUGR were selected most women were primigravidae, 20-34 years, and from low socio-economic status. 25 women (13.8%) had oligohydramnios (AFI <5). Of these women, 24 had an abnormal CPR, 1 normal CPR. 47% with abnormal CPR had caesarean for fetal distress. Birth weight was <1.5 kg in 14.4% of patients all of whom were in the abnormal CPR group. 7.5% had an Apgar <7; all these babies were in the abnormal CPR group. 43.9% of babies from the abnormal CPR group needed resuscitation. 79% of the abnormal CPR group babies needed NICU admission.

CONCLUSION
Utilization of only UA and MCA indices may cause unnecessary early intervention in some cases. CPR can help triage pregnancies in need of termination while prolonging those which are relatively stable so as to gain more time fetal maturity and cervical ripening. CPR can predict the perinatal outcome of IUGR pregnancies.

KEYWORDS
Doppler, CPR, USG, IUGR, Perinatal outcome.

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INTRODUCTION: ‘Doppler velocimetry’ as a noninvasive method of measuring changes in blood flow velocity in human pregnancy was first reported in 1971 by Fitzgerald and Drumm who used it to study umbilical vessels. Today, even small vessels can be studied with great accuracy and it is an invaluable tool in antenatal fetal surveillance. Randomised Controlled Trials (RCTs) have shown that use of Doppler indices in the management of Intrauterine Growth Restriction (IUGR) cases is associated with a significant reduction in a perinatal mortality rate. Deterioration of various Doppler indices, precedes abnormal Biophysical Profile (BPP) by 1-2 weeks. Traditionally, umbilical artery indices have been used to determine management options and an elevated S/D (Systolic/Diastolic) ratio would lead to a consideration of termination of pregnancy. However, this only reflects the placental status.
What is the fetal response to this increasing placental insufficiency? Studying the MCA indices in relation to the UA indices (The cerebroplacental ratio (CPR)) gives us an idea of the fetal response to the placental status and thus is potentially more advantageous in predicting fetal outcome.7

AIMS OF THE STUDY:
- To evaluate the role of UA and MCA Doppler in IUGR foetuses.
- To compare the impact of worsening CPR against the conventional indices (UA and S/D ratio) in predicting adverse fetal outcomes.

MATERIALS AND METHODS: The study was conducted as a prospective cohort study of cases of IUGR in the Department of Obstetrics and Gynaecology in Calicut Medical College in association with Department of Radiodiagnosis from January 2013 to December 2013. From among the antenatal women registered to our department, 180 cases of clinically diagnosed IUGR were selected for the study. Personal and demographic data, detailed obstetric history (Including history of PIH, GDM, DM, Chronic hypertension), details of present pregnancy (Including LMP, T1, USG) were recorded.

Clinical findings, obstetric exam findings (Including fundal height) were recorded and lab investigation results were noted. Those patients whose fundal height showed a disparity of at least 3 cm were included in the study.

EXCLUSION CRITERIA: Irregular cycles, unknown last menstrual period, those with early growth restriction from second trimester, history of viral exanthemas, intake of antiepileptics, antipsychotics, anticoagulants, congenital malformations, and twins. Obstetric Ultrasound (USG) was performed in all selected cases with Doppler evaluation of UA (Free loop) and Fetal MCA (Middle section) at the Department of Radiodiagnosis in GMC, Calicut. The S/D ratio, RI, PI values were obtained and CPR calculated. All cases were kept under surveillance and decision for termination was based on umbilical artery S/D ratios as per the protocol then in place. (CPR was not used for clinical management).

Outcome of pregnancy was recorded in detail including nature of labour, birth weight, Apgar score, IUD, NND, and other neonatal complications; (Hypocalcaemia, Hypoglycemia, Hyperbilirubinemia, ICH, HIE, MAS). These details were entered in a proforma and the data was statistically analysed and evaluated by SPSS. An abnormal CPR was defined as <1. The sensitivity, specificity, and predictive values for predicting adverse outcomes were calculated. Fetal adverse outcomes were categorized under major (IUD, NND, HIE, IVH, MAS, NEC, Pulmonary haemorrhage) and minor (Non-reactive CTG, Caesarean for fetal distress, Apgar <7 at 5 min, Need of resuscitation, NICU admission, Hypoglycemia, Hyperbilirubinemia, etc.) adverse outcomes.

RESULTS: 180 clinically detected cases of IUGR were selected for the study. 91.1% women were in the 20-34 age group (7.8% <20, 1.1% >35).
66% were in the low socio-economic status group while 33.3% were in the middle socioeconomic group.63% were primigravidas and around 1% was grand-multiples. Thus, majority of the IUGR cases were primigravidas aged 20-34 years hailing from a low socio-economic group. There were identifiable risk factors in 44.4% of cases.8

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Risk Factor</td>
<td>100</td>
<td>55.6%</td>
</tr>
<tr>
<td>Risk Factor present</td>
<td>80</td>
<td>44.4%</td>
</tr>
<tr>
<td>1. Pregnancy-induced hypertension (PIH)</td>
<td>45</td>
<td>56.25%</td>
</tr>
<tr>
<td>2. Gestational diabetes mellitus (GDM)</td>
<td>10</td>
<td>12.5%</td>
</tr>
<tr>
<td>3. PIH and GDM</td>
<td>5</td>
<td>6.25%</td>
</tr>
<tr>
<td>4. Previous IUGR</td>
<td>10</td>
<td>12.5%</td>
</tr>
<tr>
<td>5. Heart disease</td>
<td>6</td>
<td>7.5%</td>
</tr>
<tr>
<td>6. Miscellaneous</td>
<td>4</td>
<td>5%</td>
</tr>
</tbody>
</table>

Table 1: Risk Factor Association with IUGR

Most common was gestational hypertension. The miscellaneous group (5%) included one case of SLE, two cases of placenta previa, one case of neurofibromatosis with cervical myelopathy. Among 180 cases, 102 had a normal AFI, 53 women had AFI 5-10, 21 women had an AFI <5 and 4 women had no demonstrable liquor pockets. Thus, 25 women (13.8%) had oligohydramnios (AFI <5).

Liquor Status | Normal AFI | AFI 5-10 | AFI <5 | No Demonstrable Liquor Pockets
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Total Number</td>
<td>102 (56.6%)</td>
<td>53 (29.4%)</td>
<td>21 (11.6%)</td>
<td>4 (2.2%)</td>
</tr>
</tbody>
</table>

Table 2: Liquor Status Amongst IUGR

(29% were Normal AFI; 57% were AFI 5-10, 29% were AFI <5.)

(OF these 25 women with oligoamnios; 24 had an abnormal CPR, 1 normal CPR.)

14.4% of women had an abnormal BPP (of which only one patient with oligoamnios was in the normal CPR group—remainder fell in the abnormal CPR group). The sensitivity, specificity, and predictive values of BPP were as follows:

<table>
<thead>
<tr>
<th>INDEX</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>UA S/D</td>
<td>63.8</td>
<td>62.9</td>
<td>53.4</td>
<td>72.3</td>
</tr>
<tr>
<td>MCA S/D</td>
<td>60</td>
<td>56</td>
<td>48.8</td>
<td>66.7</td>
</tr>
<tr>
<td>UA RI</td>
<td>62.5</td>
<td>68.5</td>
<td>54</td>
<td>75.5</td>
</tr>
<tr>
<td>MCA RI</td>
<td>44.3</td>
<td>87.2</td>
<td>71.2</td>
<td>72.9</td>
</tr>
<tr>
<td>UA PI</td>
<td>40.3</td>
<td>87</td>
<td>67.4</td>
<td>68.6</td>
</tr>
<tr>
<td>MCA PI</td>
<td>45.8</td>
<td>88.9</td>
<td>73.3</td>
<td>71.1</td>
</tr>
</tbody>
</table>

Table 3: The Diagnostic Accuracy of IUGR

Of the 180 women, almost 50% (n=88) had a caesarean, with one third (n=26) of these being for fetal indications like MSAF, fetal distress, presumed fetal jeopardy. 17 women had a caesarean for severe preeclampsia with/without other factors (Whilst comparing the normal CPR with the abnormal CPR group, 47% with abnormal CPR had a birth weight <2.5 kg birth weight, 27% of babies in the normal CPR group were <2.5 kg birth weight, 27% of babies required NICU admission. Of these, 79% belonged to the abnormal CPR group. 43 babies had neonatal complications, which included 14 with symptomatic hypoglycemia, 12 with neonatal hyperbilirubinemia.

The diagnostic accuracy of the CPR RATIO calculated by using S/D, RI, PI in predicting perinatal outcomes was also compared.

<table>
<thead>
<tr>
<th>CPR</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPR S/D</td>
<td>53</td>
<td>81.5</td>
<td>63</td>
<td>74.6</td>
</tr>
<tr>
<td>CPR RI</td>
<td>64.5</td>
<td>83.3</td>
<td>69</td>
<td>80.4</td>
</tr>
<tr>
<td>CPR PI</td>
<td>66.7</td>
<td>85.2</td>
<td>75</td>
<td>79.3</td>
</tr>
</tbody>
</table>

Table 5: Diagnostic Accuracy for various CPR

DISCUSSION: In our study of 180 women with IUGR, we found that most cases belonged to the age group of 20-34 years. Most were primiparas and most were from low socio-economic status. Risk factors were identified in 44.4% and majority of these (56.25%) had hypertension as the risk factor. 13.8% of women had an abnormal Amniotic Fluid Index (AFI) and 14.4% had an abnormal Biophysical profile (BPP) whereas almost 50% had an abnormal MCA S/D ratio or UA S/D ratio. This shows that an abnormal Doppler velocimetry precedes changes in BPP in the IUGR babies and can be given an earlier indication of need for termination. When the CPR was analysed, only 35% of women had a CPR <1 and it was this group that showed a statistically significant increase in various morbidity creating parameters like.

- Caesareans for fetal distress (47% as opposed to 28.5% in normal CPR group).
- Low birth weight.
  - a) All babies in ‘CPR <1’ group were <2.5 kg vs. 52% in the ‘normal CPR’ group who were >2.5 kg.
  - b) All babies (n=20) <1.5 kg were in the abnormal CPR group vs. none in the normal CPR group.
- Of babies in the 1.5-2.5 kg birth weight, 27% were in the abnormal CPR group vs. 63% in the normal GPR group.
- Low Apgar scores; all 13 babies with Apgar <7 cm were in the abnormal CPR group (vs. none in the normal CPR group).
- Need for neonatal resuscitation.

Of the babies who needed neonatal resuscitation, 86% were in the abnormal CPR group (vs. 13.2% in the normal CPR group). Only, 3.4% of the normal CPR group required resuscitation whereas 43.9% of the abnormal CPR group who required resuscitation.
27% of the babies from the total study group required admission. Of these, 79% were from the abnormal CPR group and 21% were from normal CPR group. Of all the babies in the abnormal CPR group, almost 65% required NICU admissions.

All the above parameters were found to be statistically significant. Also, neonatal complications like HIE stage II, III, symptomatic hypoglycaemia, meconium aspiration syndrome, neonatal hyperbilirubinemia, and intracranial haemorrhage were more in the abnormal CPR group though not statistically significant in the present study.

However, larger studies maybe required to establish statistical significance. There were 10 perinatal deaths compromising of 7 cases of intrauterine deaths and 3 cases of neonatal deaths, all of whom were from the abnormal CPR group. When comparing the diagnostic accuracy of abnormal UA S/D ratio with CPR in predicting adverse perinatal outcome, this shows that abnormal CPR can identify a subgroup of babies in the abnormal UA Doppler velocimetry group who are at a greater risk of poor perinatal outcome thus warranting earlier termination.\(^{(1,4,7)}\) As a corollary, the babies with normal CPR may not be as susceptible to adverse perinatal outcome and a further period of antenatal surveillance rather than immediate termination maybe opted for especially at earlier gestational ages where neonatal survival cannot be assured.

**CONCLUSION:** Doppler velocimetry is one of the best noninvasive tools in detecting foetal growth restriction and predicting perinatal complications. It can be used in decision making when IUGR is diagnosed to achieve optimal perinatal outcome.\(^{(10)}\) However, utilization of only umbilical artery and middle cerebral artery indices may cause unnecessary early intervention in some cases.\(^{(3)}\) where a few more days of intrauterine life may be beneficial for the baby or waiting for an additional week may make the cervix more favourable and increase the chance of a vaginal delivery. This subgroup maybe identified using cerebroplacental ratio, which combines MCA and UA parameters, thus incorporating not only the placental status, but also the fetal response to the given placental status into the decision-making algorithm.

**REFERENCES**