Doppler Triple-vessel Wave Pattern as a Screening Method for Prediction of Perinatal Outcome in Pregnancy-induced Hypertension

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ABSTRACT

Introduction: Triple-vessel Doppler flow velocity waveforms are widely used in obstetric practice. It has been studied for predicting a variety of adverse fetal outcomes. This is a descriptive type of observational study aimed to assess the role of umbilical artery (UA), middle cerebral artery (MCA), and uterine artery Doppler in pregnancy-induced hypertension (PIH) patients and their perinatal outcome.

Materials and methods: This study was conducted on 200 pregnant women (100 cases and 100 control) attending antenatal clinic after the assessment of inclusion and exclusion criteria over a period of 1 year. After an informed consent, 100 women with period of gestation >30 weeks diagnosed as PIH were subjected to transabdominal ultrasound during which triple-vessel Doppler waveforms were taken. Those patients with abnormal report underwent repeat Doppler and were observed for any changes indicating adverse fetal outcomes.

Results: Out of 100 cases studied, 71 showed positive Doppler indices in any of the three vessels studied. The remaining 29 cases showed normal Doppler indices in all the three vessels studied. Among abnormal 71 cases, 56, 52, and 39 cases had abnormal MCA, uterine artery, and UA Doppler indices respectively. The specificity and the positive predictive value (PPV) of UA pulsatility index (PI) was more, as compared with the specificity and PPV of MCA PI and also cerebroplacental ratio.

Conclusion: Triple-vessel Doppler study is a safe, noninvasive technique, easy to perform, easy to interpret, and hence, most valuable tool in the management of high-risk pregnancy. Thus, it is very useful in predicting adverse perinatal outcome in PIH pregnancies.

Keywords: Cerebroplacental ratio, Doppler velocimetry, Perinatal outcome, Pregnancy-induced hypertension, Umbilical artery, Uterine artery.


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INTRODUCTION

Although hypertensive disorder of the pregnancy is a major cause for maternal morbidity and mortality, little is known about its etiology and prophylactic treatment. The struggle to find an effective screening method for prompt diagnosis, to provide an effective treatment, and to prevent complications continues.1 Pregnancy-induced hypertension (PIH) is mainly seen in the first trimester and affects 2 to 5% of all pregnancies.2 Pregnancy-induced hypertension is caused by vasospasm and endothelial pathology, which in turn cause decreased perfusion of the organs leading to intrauterine growth retardation (IUGR), which is commonly associated with it.

Last 15 years have shown that increased impedance in the flow of the uterine arteries is due to impaired trophoblastic invasion of the maternal spiral arteries due to PIH.3-9 This leads to impaired placental circulation, which becomes a high resistance flow. This results in impaired uteroplacental blood flow manifestations, such as IUGR, oligohydramnios, placental abruption, fetal hypoxia, perinatal death, and nonreassuring fetal heart status.10,11 This can be very well assessed via ultrasonography (USG Doppler velocimetry). Doppler velocimetry is a rapid noninvasive test that provides valuable information about hemodynamic situation of the fetus. Doppler ultrasound evaluation has grown leaps and bounds and it may be considered as one of the most important achievements of modern day obstetrics.

Doppler evaluation of the cerebral artery is of huge importance as it gives the status of fetal hypoxia. The diagnostic prowess of the middle cerebral artery (MCA), umbilical artery (UA), and renal Doppler artery has been evaluated by various studies, including studies done by Fong et al12 and Zha et al.13 Uterine artery
has been rigorously assessed for the presence of a diastolic notch as it is associated with poor placental circulation. Prolonged hypoxia leads to the blood being diverted to the heart and other organs, whereas the fetal brain undergoes an insult. Recent studies have pointed out that the cerebroplacental ratio (CPR) and the pulsatility index (PI) of MCA and UA give a better prognostic picture than the other indices.

In this study, we have assessed the fetal outcome of patients with normal and abnormal Doppler velocimetry and tried to validate the previous studies in order to find a good and effective screening method for the early diagnosis, which will help in the prompt treatment of this condition.

MATERIALS AND METHODS

This study was performed between October 2014 and October 2015 in NIMS Medical College, Jaipur, India, where a total of 200 patients were included in the study, out of which, 100 were cases and 100 were control. The cases constituted of patients having PIH, whereas the control group did not have PIH. It was a descriptive type of observational study.

All antenatal cases more than 30 weeks of gestation with singleton pregnancies, with history and physical findings suggestive of PIH and those giving consent were included in this study.

All high-risk pregnancies with severe anemia, cardiovascular diseases, multiple gestations, congenital anomalies, renal disease, Rh-negative pregnancies, essential hypertension prior to pregnancy, and intrauterine death at first Doppler examination were excluded from the study.

A detailed explained consent was taken from all the patients. Doppler USG was done by a single radiologist in all the patients. Pulsed Doppler was done in all the patients in the infant hypoxic state and the vessels were localized. Criteria for various arteries included:

- **Uterine artery**: The uterine artery was seen crossing the external iliac artery, just after its origin from the internal iliac artery and this point was taken as the sampling point.
- **Umbilical artery**: Doppler signals were acquired from different points in cord, usually from midportion of cord.
- **Middle cerebral artery**: MCA was visualized in transverse axial view of fetal head at a slightly more caudal plane than the one used for biparietal diameter.

The gestational age was calculated based on the last menstrual period (LMP), or the USG biometry performed before the 20th week if the LMP was uncertain or not known or an ultrasound in first trimester was not performed. The Doppler was repeated at an interval of 1, 2, or 4 weeks, but the findings of the last Doppler were considered for the study. The patients were followed up till delivery and the results of the pregnancy were noted.

The outcome criteria included: Birth weight (less than 10th percentile), perinatal death, emergency lower-segment cesarean section (LSCS) for fetal distress, low APGAR score (5 minutes APGAR score less than 7), and admission to neonatal intensive care unit (NICU) for complications of low birth weight (LBW). The pregnancy was considered to be of an adverse outcome if any of the above-mentioned criteria was fulfilled.

The results were assessed using the statistical analysis software, Statistical Package for the Social Sciences, version 20. The statistical analysis was done using paired t-test and the chi-square test and the level of significance of diastolic notch was found if \( p < 0.05 \) of diastolic notch and that of resistivity index, PI, and S/D ratio was determined by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Association between nominal/categorical variables was assessed using chi-square test; \( p \)-value < 0.05 was taken as significant.

RESULTS

Out of the 200 patients included in this study, maximum patients, i.e., 48% (n = 48) and 46% (n = 46), were in the age group of 20 to 24 years in the study and control groups respectively. Majority (55%) of the cases were term and 45% (n = 45) and 13% (n = 13) of patients had preterm delivery in study and control group respectively. In the study and control group, 54 and 60% of patients respectively, were primigravida, indicating high risk of PIH in primigravidas (Graph 1). Out of 30 patients with oligohydramnios, 29 had abnormal Doppler as compared with 42 of 70 patients with normal amniotic fluid index.

Of the 100 cases with PIH, 41% had IUGR, 2% had ascites, and 1% developed HELLP (Hemolysis, Elevated

![Graph 1: Pregnancy outcome in the study and control groups](image-url)
Liver enzymes, and Low Platelet count) in comparison to control group where only 2% of patients had IUGR. In the study group, 20 (80%) out of 25 patients who underwent emergency LSCS had abnormal Doppler. Of the 71 cases with abnormal Doppler, 52 delivered within 24 to 48 hours and 10% delivered in less than 24 hours. In addition, 83% of the cases had adverse pregnancy outcome in the form of LBW, low AFGAR, NICU admission, perinatal death, or LSCS in comparison to the control group where only 16% had adverse pregnancy outcome (Graph 2).

In the study group, 65% of neonates (n = 65) had birth weight <2.5 kg, 37 neonates were admitted to NICU, 24 had 5 minutes AFGAR score of less than 7, 23 were born by emergency cesarean section for fetal distress, and 26 had neonatal death. In the study group, 65% of the neonates had LBW as compared with 16% in the control group. Out of 100 cases, 71 had an abnormal Doppler, and 36 of 39 cases with abnormal UA Doppler indices had adverse perinatal outcome, showing significant association between UA Doppler and perinatal outcome. Of 56 cases with abnormal MCA Doppler indices, 39 had adverse perinatal outcome. Among 41 cases with diastolic notch in UA, 68.29% (n = 28) of patients had adverse pregnancy outcome; 100% mortality was seen in 18 cases with absent end diastolic flow (AEDF) and 2 cases with reversed end diastolic flow (REDF).

Among all the Doppler indices of the three vessels, UA had the highest specificity and PPV. Cerebroplacental ratio had the highest sensitivity and diagnostic accuracy (Graph 3).

**DISCUSSION**

Pregnancy-induced hypertension is associated with increased risk of perinatal morbidity, mortality, and impaired neurological development.1,2 In this study, 48 (48.00%) women were aged between 20 and 24 years. Of the 100 pregnant women in the study group, 54 (54%) were primigravida and 27 (27%) were gravida 2, which was similar to that quoted by Kurdi et al,14 Martin et al,15 and Papageorghiou et al.16

Out of 100 women in the study group, 41% women developed IUGR along with PIH and this was comparable to the study of Coleman et al17 (26.7%) and higher than that of Kurdi et al14 (16.5%), Bewley et al18 (12.9%), and Irion et al19 (11%). High prevalence of IUGR and pre-eclampsia is due to demographic variation of study population characteristics and their geographical variation as rural population have nutritional deficiency (above studies involved urban population) and due to biphasic screening method of the current study.

In this study, all the Doppler USGs were performed by a single radiologist. This was done to avoid any interobserver variation.

Umbilical artery and MCA Doppler ultrasound clearly depicts 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 leading to growth-retarded fetus. Middle cerebral artery Doppler has enabled the confirmation of brain-sparing effect in PIH and IUGR. Hence, we chose the UA PI, MCA PI, and MCA PI/UA PI, i.e., CPR as the tool for predicting the perinatal outcome in patients with PIH with or without IUGR.

We studied the Doppler index of UA only after 30th week, in agreement with Schulman11 and Gramellini.20 We believe that it is difficult to define normal or abnormal umbilical flow velocity before 30th week, with the exception of AEDF velocity after 20th week.

We studied the Doppler index of MCA because it is the most accessible artery to see the cerebral redistribution as it is the main branch of the circle of Willis and carries 80% of the blood flow to the ipsilateral cerebral hemisphere, a
constant 3 to 7% of cardiac output throughout gestation. The MCA PI and UA PI values for the corresponding gestational age were compared with reference values given by Harrington et al.21 normograms. The MCA PI was considered abnormal when it was less than 5th percentile for that gestational age and UA PI was considered abnormal when it was more than 95th percentile for the corresponding gestational age. It is possible to use a single cutoff value for CPR after 30th week because cerebral-umbilical Doppler ratio does not vary significantly between 30th and 40th weeks as reported by Vlaimiroff et al.22 who observed a significant difference in CPR only between weeks 26 and 38. Arbeille et al.23 also found the CPR constant during the pregnancy and suggested 1 as the cutoff value and all values below 1 were considered abnormal. We considered the study of Gramellini et al.20 that showed CPR < 0.18 as abnormal. In the study group, 65% of neonates (n = 65) had birth weight < 2.5 kg. Of the 100 neonates, 37 neonates were admitted to NICU, 24 neonates had 5 minutes APGAR score of less than 7, and 23 babies were born by emergency cesarean section for fetal distress. There were 26 neonatal deaths. Of the 26 neonatal deaths, 2 cases had REDF and 18 had AEDF.

Umbilical artery (Table 1): The UA PI effectively rules out the possibility of an adverse perinatal outcome when it is normal. There is likelihood of adverse perinatal outcome in growth-retarded fetus with abnormal UA PI. It provides useful information for differentiating fetuses already compromised or likely to become compromised from those that are noncompromised. The findings agree with those of Harrington et al.21 that UA can be normal in term and near-term with abnormal MCA.

Middle cerebral artery (Table 2): This study agrees with Fong et al.12 that MCA PI is less specific than CPR and UA PI. Among several published normograms for MCA PI,24-26 the cutoff values for an abnormal MCA PI are similar up to about 30 weeks gestational age but differ after 32 weeks. The normograms we chose to use for analysis are from the largest published cross-sectional study by Harrington et al.21 High PPV of MCA PI can be attributed to the less false-positive values. The high NPV is more useful in ruling out the possibility of adverse perinatal outcome.

<p>| Table 1: Performance characteristics of umbilical artery Doppler indices in present study group and reference studies |
|---------------------------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Fong et al.12 (%)</th>
<th>Gramellini et al.20 (%)</th>
<th>Present study (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>44.7</td>
<td>64</td>
<td>60.2</td>
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<tr>
<td>Specificity</td>
<td>86.6</td>
<td>90.7</td>
<td>88.56</td>
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<tr>
<td>Positive predictive value</td>
<td>54</td>
<td>72.7</td>
<td>81.78</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>81.7</td>
<td>86.7</td>
<td>80.34</td>
</tr>
</tbody>
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<p>| Table 2: Performance characteristics of MCA Doppler indices in present study group and reference studies |
|---------------------------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Fong et al.12 (%)</th>
<th>Gramellini et al.20 (%)</th>
<th>Present study (%)</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>72.4</td>
<td>24</td>
<td>76.46</td>
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<tr>
<td>Specificity</td>
<td>58.1</td>
<td>100</td>
<td>79.96</td>
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<tr>
<td>Positive predictive value</td>
<td>37.7</td>
<td>100</td>
<td>80.12</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>85.7</td>
<td>77.30</td>
<td>79.89</td>
</tr>
</tbody>
</table>

<p>| Table 3: Performance characteristics of CPR in present study group and reference studies |
|---------------------------------|----------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Fong et al.12 (%)</th>
<th>Gramellini et al.20 (%)</th>
<th>Present study (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>51.3</td>
<td>68</td>
<td>89</td>
</tr>
<tr>
<td>Specificity</td>
<td>80.6</td>
<td>98.4</td>
<td>80</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>48.1</td>
<td>94.4%</td>
<td>77</td>
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<tr>
<td>Negative predictive value</td>
<td>82.5</td>
<td>88.8</td>
<td>81</td>
</tr>
</tbody>
</table>

Cerebroplacental ratio (Table 3): The highest sensitivity of CPR indicates its usefulness in ruling out the possibility of adverse perinatal outcome in PIH with IUGR when the ratio is normal for the gestational age. It indicates that the likelihood of favorable outcome is more when the CPR is normal. This study agrees with that of Chan et al.22 that the CPR is more sensitive than UA PI, but at the expense of decreased specificity.

Mortality of 100% was seen in cases with REDF and AEDF as compared with Bhatt et al.28 and Battaglia et al.29 both of which showed 50% mortality. This confirms the findings of Karsdorp et al.30 which showed that AEDF and REDF are better indicators of the adverse perinatal outcome. Studies have shown that AEDF and REDF in the UA are associated with increased perinatal mortality and morbidity.31-34

There were certain limitations to this study. These included a small number of subjects; rarity of some perinatal and neonatal complications made them difficult to evaluate and some confounding factors might still have had an effect on the results.

CONCLUSION

The primary aim of antepartum fetal surveillance is timely recognition of fetal compromise to enable appropriate intervention and to prevent further serious complications. If the fetus would otherwise die in utero, delivery might save its life, but ill-advised pre-term delivery may be followed by postnatal death.

These results in evaluating the usefulness of UA and MCA Doppler in predicting the adverse perinatal outcome in PIH and IUGR indicate that both abnormal umbilical Doppler indices and cerebral-umbilical ratio are strong predictors of adverse outcome in PIH and IUGR.
Doppler Triple-vessel Wave Pattern as a Screening Method for Prediction of Perinatal Outcome in PIH

The MCA PI alone is not a reliable indicator when used alone. The combination of umbilical and fetal cerebral Doppler indices may increase the utility of Doppler ultrasound in clinically suspected IUGR. Thus, triple-vessel Doppler study is very useful in predicting adverse perinatal outcome in PIH pregnancies when the Doppler velocimetry is abnormal.

REFERENCES


