

USG Doppler Study of Uterine, Umbilical and Foetal Middle Cerebral Arteries Among Severe Pre-Eclamptic Women and their Relation to Perinatal Outcomes

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ABSTRACT

Introduction: Pre-eclampsia is a condition in pregnancy characterized by the onset of hypertension and proteinuria after 20 weeks of gestation. This affects multiple organs in mother and also has a significant impact on the fetus. The extensive changes caused by pre-eclampsia result in complications leading to fetal jeopardy, such as placental abruption, fetal growth restriction, pre-term birth, respiratory distress and Intra uterine demise (IUD). The definitive treatment of pre-eclampsia is termination of pregnancy and initiation of treatment is crucial. Doppler ultrasonography (USG) is non-invasive and can be done along with the routine obstetric scans and is therefore considered safe and suitable for the study of blood flow alterations caused by severe pre-eclampsia. Not only would it serve as a predictive tool, it would also help plan subsequent management of the pregnancy, based on fetal health.

Aim: To study the changes in uterine, umbilical and foetal middle cerebral arteries in severe pre-eclampsia, using Doppler ultrasonography and to provide basis for use of Doppler tests in directing treatment protocol of severe pre-eclampsia

Materials and Methods: In this study, women with severe pre-eclampsia near term were selected based onset criteria and detailed history was obtained. USG Doppler was performed for each of the patients and the results were recorded. They were further followed till parturition to study the perinatal outcomes. Doppler study results and perinatal outcomes were considered together to find a correlation.

Results: It was found that 21 out of 26 patients (81%) showed abnormal Doppler results and 19 out of 26 cases (73%) suffered from adverse perinatal outcomes. 5 of them (19%) had suffered from intra uterine demise (IUD). Uterine artery showed restricted flow in 6 cases (23%), umbilical artery showed reduced flow in 12 cases (46%) and foetal MCA showed abnormal flow in 20 cases (77%).

Conclusion: There is a good correlation between doppler results and adverse perinatal outcomes and we have found that the umbilical artery flow velocimetry is the most sensitive to predict the same. A treatment plan can be initiated based on the findings to keep both mother and child safe.

Keywords: Diastolic reversal, Foetal Doppler, (IUD) Intra Uterine Demise

INTRODUCTION

Pre-eclampsia is a disorder in pregnancy characterized by the onset of hypertension and proteinuria after 20 weeks of gestation. It affects 2-8% of all pregnancies [1]. The WHO states that it is 7 times more common in developing countries than the developed ones [2]. In India, the incidence of pre-eclampsia is higher owing to the presence of risk factors such as teenage pregnancy, low socio-economic status etc.

The underlying pathology in pre-eclampsia is faulty placentation and widespread vasoconstriction resulting in endothelial damage. This affects multiple organs in the mother and also has a significant impact on the fetus. Increased resistance to blood flow in uterine arteries indicates diminished materno-placental perfusion. Reduced blood flow through umbilical arteries is also critical, depicting compromised placento-umbilical circulation, When there is fall in diastolic flow through

umbilical arteries, fetal compensation occurs in the form of centralization of flow (brain-sparing effect) [3]. By this effect, the blood flow through the fetal middle cerebral artery (MCA) is increased. However, in advanced cases, the umbilical artery shows absent or reversed diastolic flow. In such a situation, there is decompensation, worsening fetal hypoxia and acidosis, ultimately leading to imminent intra-uterine demise [4].

The definitive treatment of pre-eclampsia is separation of placenta from its bed i.e. termination of pregnancy [5]. Timely initiation of treatment is crucial. If fetal distress is detected, emergency induction of labour or Caesarian delivery is needed to keep the mother and child safe. Doppler ultrasonography (USG) is non-invasive and can be done along with the routine obstetric scans. We use it to study the circulation through maternal, placental and foetal vasculature. USG Doppler is therefore considered safe and suitable for the study of blood flow alterations caused by severe pre-eclampsia.

Need for Study

Pregnancy-induced hypertensive disorders account for 14% of maternal deaths worldwide [6]. Though the vascular changes happening in severe pre-eclampsia begin as early as the second trimester, the advanced changes which leads to deleterious effect occur at or near term and these changes can be picked up by doppler studies only in an advanced stage. Hence, this study is done near term can be used to conclude whether the pregnancy needs to be terminated or allowed to reach term. Though these changes start as early as second trimester not all cases progress to severe form of pre-eclampsia.

Despite the ominous effects of severe pre-eclampsia, reliable tests to predict the complications are insufficient. Though, the subject is being researched in several countries worldwide [7-9], there is dearth of evidence regarding the same, especially in India [10]. In India, a sizable portion of population falls under low socioeconomic status, antenatal visits by pregnant women are irregular or almost absent. In fact, quite a number of pregnancies are unbooked. As a result, many severely pre-eclamptic women land-up at a tertiary centre with severe complications near term and with inadequate obstetric history. The use of a USG Doppler vascular studies to identify complications would be immensely beneficial. Not only would it serve as a predictive tool, it would also help plan subsequent management of the pregnancy, based on fetal health.

Deleterious changes due to severe pre-eclampsia lead to fatal complications such as placental abruption, fetal growth restriction, intra uterine demise and acute respiratory distress in the baby after birth.

Though the vascular changes happening in severe pre-eclampsia begin as early as the second trimester, the advanced changes which leads to deleterious effect occur at or near term and these changes can be picked up by doppler studies only in an advanced stage. Hence this study is done near term can be used to conclude whether the pregnancy needs to be terminated or allowed to reach term. Though these changes start as early as second trimester, not all cases progress to severe form of pre-eclampsia.

MATERIALS AND METHODS

This was a prospective study, conducted in Vanivilas Hospital, Bangalore, India over the period of 2 months between September 1, 2014 to October 30, 2014. Twenty six severely pre-eclamptic women near term and their neonates, who were admitted in this hospital were considered for the study, after obtaining clearance from the ethical committee of the Institution. Women admitted with severe pre-eclampsia were chosen on the basis of inclusion and exclusion criteria. Informed consent was obtained from all the participants. Detailed history of the patient including – name, age, in depth record of gestational history as well as history pertaining to pre-eclampsia was recorded.

Inclusion Criteria

Pregnant women who experienced one or more of the following:

Blood pressure ($\geq 160/110$ mmHg).

Severe proteinuria ($\geq 3+$ in random samples).

Evidence of CNS dysfunction (headaches, visual disturbances).

Pain in the epigastrium.

Renal dysfunction (oliguria or creatinine > 1.5 mg/dl).

Pulmonary oedema.

HELLP syndrome

Oligohydramnios or severe intrauterine growth restriction.

Exclusion Criteria

Women who have:

Chronic hypertensive disorders.

Pre-existing liver or kidney disease.

Multiple gestations.

Neonates with gross congenital malformations.

All pregnant women admitted with severe pre-eclampsia underwent various investigations such as urine albumin, RFT, DIC Profile (including platelet count), LFT, LDH profile and USG for oligo hydramnios/IUGR. They were not performed as part of this project. The information obtained from these tests was used for selecting the study population.

METHOD OF DATA COLLECTION

Doppler Study: Doppler ultra-sonography was performed on all the study participants. The uterine, umbilical and fetal middle cerebral arteries were studied using appropriate probes (high-frequency linear array transducer).

The reports contained the following haemodynamic parameters:

- RI-Resistive index = Systole- diastole / Systole
- PI-Pulsatility index = Peak systolic velocity –End diastolic velocity / time averaged velocity
- S/D- Systolic to diastolic ratio

The parameters were then each compared to reference values for detecting changes and abnormalities:

1. Uterine artery (Ut A) –

- RI:PI:S/D -abnormal if > 95th percentile [11, 12]

2. Umbilical artery (UA) –

- RI:PI: S/D -abnormal if > 95th percentile [13]

3. Foetal middle cerebral artery (MCA) –

- RI:PI: S/D -abnormal if <5th percentile [14]

Foetal Outcomes: The neonates in Set 2 were observed to study outcome of pregnancy. Foetal asphyxia (Low birth weight), respiratory distress, need for admission to Neonatal ICU (NICU) and perinatal death were taken as adverse perinatal outcomes.

DATA ANALYSIS

Based on information obtained from the above investigations, the women in Set 1 were categorized into 4 groups:

A – Mother with normal Doppler results and normal perinatal outcome

B – Mother with normal Doppler results but adverse perinatal outcome

C – Mother with abnormal Doppler results but normal perinatal outcome

D – Mother with abnormal Doppler results and adverse perinatal outcome

Furthermore, the Doppler results of the arteries were compared with foetal outcome to study the sensitivity of each.

STATISTICAL METHODS

Descriptive charts and tables were used to study the blood flow changes and perinatal outcomes. The p-value (<0.10 considered significant) was used to analyze the sensitivity of each artery in predicting adverse perinatal outcome.

RESULTS

Out of 44 patients, 11 patients opted to be discharged against medical advice and shifted to a private hospital for

delivery. Seven patients had not delivered by the end of the study period. Hence, the sample size was 26 excluding the above 18 patients.

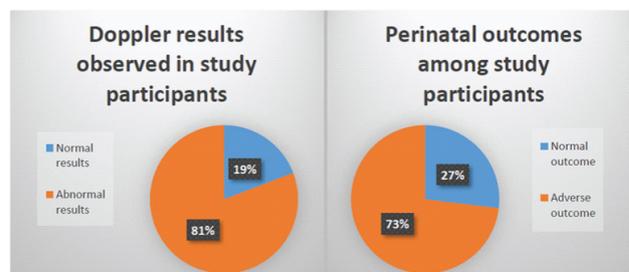
It was found that 21 out of 26 patients (81%) showed abnormal Doppler results and 19 out of 26 cases (73%) suffered from adverse perinatal outcomes. 5 of them (19%) had suffered from intra uterine demise (IUD) [Table/Fig-1].

The patients were categorized into 4 groups as mentioned in methodology based on Doppler results and perinatal outcomes. It was found that 16 out of 26 cases (62%) had abnormal Doppler study results and also suffered from adverse perinatal outcomes [Table/Fig-2].

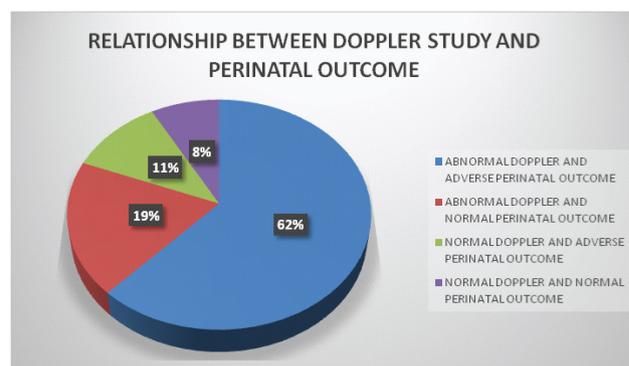
Uterine artery showed restricted flow in 6 cases (23%), umbilical artery showed reduced flow in 12 cases (46%) and foetal MCA showed abnormal flow in 20 cases (77%) [Table/Fig-3].

Furthermore, each artery and its relation to perinatal outcome was studied, we found that umbilical artery shows significant correlation (p value ~ 0.08) with adverse perinatal outcomes [Table/Fig-4].

The specific changes in Doppler indices (PI, RI and S/D ratio) in each of the arteries was studied [Table/Fig-5], and it was found that most of the cases showed abnormal values in all the three indices.



[Table/Fig-1]: Doppler results and perinatal outcomes among the study participants.



[Table/Fig-2]: Relationship between doppler study and perinatal outcome.

| Artery studied | Number of cases with abnormalities (out of 21) |
|-----------------|--|
| Ut A only | 0 |
| UA only | 1 |
| MCA only | 7 |
| Ut A + UA only | 0 |
| Ut A + MCA only | 2 |
| UA + MCA only | 7 |
| Ut A + UA + MCA | 4 |

[Table/Fig-3]: Distribution of abnormal Doppler study in severe pre-eclampsia.
Ut A –Uterine artery; UA-Umbilical artery ; MCA-Middle cerebral artery

| | | Normal perinatal outcome | Adverse perinatal outcome | p-value |
|------------------|----------|--------------------------|---------------------------|---------|
| Uterine Artery | Normal | 5 | 16 | 0.58 |
| | Abnormal | 2 | 3 | |
| Umbilical artery | Normal | 6 | 8 | 0.08* |
| | Abnormal | 1 | 11 | |
| Foetal MCA | Normal | 2 | 4 | 0.55 |
| | Abnormal | 3 | 17 | |

[Table/Fig-4]: Relation between Doppler changes and perinatal outcomes.
*p < 0.10 considered significant

| Abnormal artery | RI only | PI Only | S/D only | RI & PI | PI & S/D | RI & S/D | PI,RI&S/D |
|-----------------|---------|---------|----------|---------|----------|----------|-----------|
| Uterine A | - | 1 | - | 1 | - | - | 4 |
| Umbilical | - | 2 | - | 2 | 1 | - | 7 |
| Fetal MCA | - | 3 | - | 1 | 1 | 1 | 15 |

[Table/Fig-5]: Specific changes seen in severe pre-eclampsia.
RI-Resistance Index, PI-Pulsatility index, S/D- Systolic to diastolic ratio

| | Uterine Artery | Umbilical artery | M C A |
|----------|----------------|------------------|-------|
| Mean RI | 0.73 | 0.87 | 0.66 |
| Mean PI | 1.87 | 1.62 | 1.07 |
| Mean S/D | 4.9 | 5.20 | 2.84 |

[Table/Fig-6]: Mean value of the Doppler indices in patients with abnormal Doppler results.

DISCUSSION

As observed from our study, severe pre-eclampsia was associated with abnormal Doppler results in 81% of cases. This implies that the disease process has significant effect on maternal, placental and foetal vasculature. But Li H and Gudnason et al., reported that only 25% of pre-eclampsia in their study had abnormal uterine artery Doppler in the third trimester [15]. Uterine artery undergoes endotheliosis leading to restricted blood flow. Umbilical artery also shows reduced flow secondary to blood vessel damage. Foetal MCA increases blood flow as a compensatory effort to salvage perfusion to vital organs.

Abnormal MCA/UA PI Doppler ratio is strongly correlated with worse foetal prognosis. In normal pregnancies the diastolic component in the cerebral arteries is lower than in the umbilical arteries at any gestational age [16]. Therefore, the cerebrovascular resistance remains higher than the placental resistance and the MCA/UA PI is greater than 1. The index becomes less than 1 if the flow distribution is in favour of the brain in pathological pregnancies [16].

From our study, we see that severe pre-eclampsia is associated with adverse outcomes in 73% of the cases. This shows that pre-eclampsia has a detrimental effect on foetal health. Reduced perfusion causes hypoxia and oligo-hydramnios. This leads to intra-uterine growth restriction. In order to protect the child and mother from further harm, the baby is delivered early. However, in many cases the management measures are initiated too late leading to IUD. Even in our study 19% of the cases suffered from IUD. Since, our study was conducted in pregnant patients with approaching term, it helped in explaining the prognosis and deciding the management.

In 62% of the cases, abnormal Doppler study was associated with subsequent adverse perinatal outcomes. Also, among the 3 arteries studied – umbilical artery shows significant correlation with adverse fetal outcomes. Uterine artery and fetal MCA donot show positive correlation with the same. Thus, third trimester umbilical artery Doppler would serve as a good predictor of adverse outcomes of pregnancy.

The mean values of the Doppler indices in the various arteries were studied in patients with abnormal Doppler and it was found there was increased resistance to flow in the umbilical and uterine arteries with decreased resistance in foetal middle cerebral artery [Table/Fig-6].

Based on umbilical artery blood flow, the treatment plan can be devised as follows:

Reduced diastolic flow – deliver the foetus within 3-4 days.

Absent diastolic flow –deliver the foetus within 24 hours

Reversed diastolic flow – deliver the foetus as soon as possible.

CONCLUSION

Women with pre-eclampsia arising after 32-34 weeks shows higher risk of perinatal complications, if uterine resistance is increased. Umbilical artery Doppler is an integral part of monitoring pregnancies with pre-eclampsia and fetal growth restriction. Adverse perinatal outcome after 34 weeks of gestation is predicted better with uterine artery Doppler. Normal uterine artery Doppler in third trimester predicts good perinatal outcome and hence is reassuring. The study was conducted in a small group of patients and because of the high variability of each case, a general recommendation for the optimal timing of delivery is not possible. Thus inclusion of uterine artery Doppler in pre-eclampsia and fetal growth

restriction will give additional information essential for management of pregnancies in third trimester.

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FINANCIAL OR OTHER COMPETING INTERESTS:

None.

Date of Online Ahead of Print: Feb 26, 2016

Date of Publishing: Apr 01, 2016