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Original research article

Correlation of USG doppler study and histopathological changes of placenta to fetomaternal outcome, in pregnancy induced hypertension: A prospective study

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Abstract

Introduction: A prospective, randomized study was designed to study the variation in the Uterine, Umbilical and Middle Cerebral artery blood flow pattern in Pregnancy Induced Hypertension along with histopathological changes in the placenta and Fetomaternal outcome.

Pregnancy induced hypertension is known to cause changes in the blood flow to the foetus due to changes in the invasion of spiral arteries and placenta.

Objectives: The objective of this study was to evaluate the histopathology of placenta and doppler changes and the correlation if any, with hypertensive disorders of pregnancy and fetomaternal outcome.

Methods: A prospective, randomized study was conducted overs period of 2 years and included 100 pregnant women with singletons and pregnancy induced hypertension with gestational ages >32 weeks, admitted to the labour ward under the Department of Obstetrics and Gynecology, in a tertiary hospital.

The following findings were noted down in all cases. The Doppler parameters and any deviation from normal, from recent ultrasound report (within 2 weeks), and the maternal condition including any development of complixatioms related to PIH were noted down. The mode of delivery and gestational age at delivery, indications for LSCS or induction if done, were noted. The babies' condition soon after delivery, APGAR, and any necessity for NICU admission, IUD was noted. The placenta was examined after delivery, for Shape of placenta, size, diameter in centimeters, weight in grams, and subjected to histopathological examination to note any depositions, calcifications or other changes.

Results: Among the 100 cases, 78% (78) were in the age group of 21–30 years, with a mean age of 26.24±4.56 (range: 18–44 years). 37% of females were booked under the institution the rest were booked elsewhere and referred to the institution. 61% of cases were primingravida; 24 were second gravida 13 were Gravida 3 and 2 cases belonged to Gravida 4.

22% belonged to the gestational age group between 32 to 34 weeks; 26% were between 34 to 37 weeks and the rest were term.

Maximum cases were of Mild Pre eclampsia (43%) followed by gestational hypertension (29%), Severe Pre eclampsia (20%) and 9 cases of eclampsia.

Maternal complications due to PIH were noted, like eclampsia (9 cases), HELLP syndrome (5 cases), PRES (Posterior Reversible cerebral Encephalopathy Syndrome, 2 cases), pulmonary edema (2 cases).

Doppler changes were found in many patients, especially with bad fetomaternal outcomes.

Histopathological changes like calcification, depositions were noted in many cases.

Conclusion: Placental morphology and histopathology are affected in hypertensive pregnancies, which might be the reason for placental insufficiency

Keywords: Gestational hypertension, preeclampsia, uterine, cerebral artery, doppler velocimetry.

Introduction

Hypertension is one of the common disorders encountered in pregnancy leading to significant morbidity and mortality [1]. Hypertension, hemorrhage and infection: this deadly triad results in large number of maternal and foetal deaths [2]. Chronic hypertension with superimposed Preeclampsia (PE) and gestational hypertension complicate up to 10% of deliveries and form most important cause of disease and mortality, according to the classification of the American College of Obstetricians and

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Gynaecologists (ACOG) [3]. Placenta plays a central role in pregnancy. It plays a vital role in the progress of the foetus in utero and thus known as the mirror of maternal and foetal status [4]. The pathology of the placenta gives the precise estimate of an infant's prenatal journey [5]. Examination of the placenta and umbilical line is important to recognise what is happening to the foetus [3]. A number of histological changes occur in preeclamptic/eclamptic placentas. Some of them are infarcts, increased syncytial knots, subchorionic fibrin deposition, calcification, hypo vascularity of the villi, cytotrophoblastic proliferation, thickening of the trophoblastic membrane, obliterative enlarged endothelial cells in the foetal capillaries, and atherosis of the spinal arteries in the placenta bed [3]. Pregnancy Induced Hypertension (PIH) has adverse effects on the health of foetus through its harmful effects on the placenta [5]. Poor placentation and endothelial dysfunction are the characteristic features of PE. It carries an increased risk of progression to eclampsia. Possibility of convulsion increases leading to complications, even mother and foetal deaths [6]. The present study was undertaken to analyse the histomorphological changes in the placentas of normal and hypertensive mothers and to study its association with birth weight. Hypertension is a common medical disorder of pregnancy approximately 70% of which are primigravidas. Preeclampsia is characterized by an imbalance between prostacycline and thromboxane production [7-10], as well as failure of the second wave trophoblastic invasion of the endometrio-myometrial vasculature. The result is abnormal uteroplacental blood flow, and this has led to the idea of using color Doppler in the evaluation and management of PIH patients. Doppler ultrasound evaluation of the mother and fetus with the study of blood flow indices provides non-invasive assessment to study uteroplacental circulation and fetoplacental circulation and hemodynamic changes and adaptation in the fetal organs in response to hypoxemia; with this, the degree of placen 1 dysfunction can be studied to know the severity of the disease.

Doppler is useful in selecting the patients for induction and trial of labor, also helps in making decisions when to intervene without increasing fetal risk. This in its effect contributes to lowering maternal morbidity and also neonatal morbidity and lowers the incidence of Caesarean sections and admission to NICU care, and incidence of prematurity. Among high risk patients, several studies suggested a significant decrease in neonatal morbidity and mortality when Doppler evaluation was a part of fetal surveillance [11]. Quality of life for both mother and the new-born has now rightly become our top priority in the field of obstetrics. It is apparent that no greater services can be provided, than ensuring that each new born is well born. The common cause of maternal morbidity and mortality are Hypertensive disorders complicating pregnancy, Haemorrhage and Infection form the deadly triad that contribute greatly to maternal morbidity and mortality. Hypertensive disorders completing pregnancy has been a recognized pathological entity since the time of Hippocrates and ancient Greeks [7]. Hypertensive disorders in pregnancy are one of the major causes of maternal and perinatal mortality and morbidity. It is one of the commonest medical disorders diagnosed by obstetricians in clinical practice [8]. It is said that pregnancy induced hypertension (PIH) contributes to death of a woman every 3 minutes worldwide3.According to National Centre for Health Statistics, Gestational hypertension was identified in 3.7% of pregnancies. It is one of the commonest medical disorders diagnosed by obstetricians in clinical practice [8].

Pregnancy is a high-flow, low resistance state of cardiovascular haemostasis associated with remarkable hemodynamic changes. A progressive fall of vascular resistance in the uterine, placental and umbilical arteries is evident with increasing gestational age, producing high end-diastolic flow. In uteroplacental circulation the main uterine artery is a branch of the internal iliac artery. At the level of the internal os of cervix, it bifurcates into the descending (cervical) and ascending (corporal) branches. At the uterine tubal junction, the ascending branch anastomoses with the ovarian artery to form an arterial arcade. The tortuous accepting uterine artery gives off approximately eight branches of arcuate arteries, which then traverses the outer one-third of the myometrium. The impedance to blood flow in both uterine arteries decreases gradually from early pregnancy until the end of second trimester. More dramatic changes occur in the second trimester, when the uterus begins to grow rapidly, thereby uncoiling the main uterine and spiral arteries. Between 26 and 28 weeks of gestation, uterine arteries reach their maximal dilatation and minimal resistance [12].

The uteroplacental flow increases throughout pregnancy from approximately 50 ml/min during early pregnancy up to 450-600 ml/min near term. During normal pregnancy, the trophoblastic cells enter the lumen of the spiral arteries, partially replacing the endothelium and progressing down up to the level of the endometrium. By 16-22 weeks gestation, trophoblasts migrates along the entire length (intramyometrial portion) of the spiral arteries and strips it of its muscular elastic coat [13].

Materials and Methods

A prospective, randomized study included 100 pregnant women with singletons admitted to the labor room with gestational ages >32weeks with hypertensive disorders of pregnancy for 2 years, admitted to the Department of Obstetrics and Gynecology, in a tertiary hospital All cases were examined for Shape of placenta, weight in grams, size, diameter in centimeters, and deposition. All pregnant females admitting to the labor room with gestational age >32 weeks and hypertensive disorder of pregnancy,

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multiple pregnancy, pregnancy with other medical disorders, and not willing to participate were excluded from the study. After obtaining approval from the institutional research ethical committee and written informed consent from a patient with hypertensive disorder having blood pressure >140/90 with singleton pregnancy >32 weeks in labor or having induction of labor were selected. Information regarding her age, address, socioeconomic status, and dietary habits were noted. USG Doppler velocimeters were measured & calculated. During USG Doppler studies parameters recorded were S/D ratio, RI in uterine, umbilical and middle cerebral artery (MCA), Pulsatility Index (PI = difference between the peak systolic and end-diastolic shift divided by the average shift (A) over the cardiac cycle. The flow velocity waveforms were considered abnormal if there existed an early diastolic notch in uterine artery (in either right or left uterine arteries) and S/D, RI exceeded 95th percentile of the range of reference; in umbilical artery if S/D, RI exceeded 95th percentile and if end-diastolic flow velocity was absent or reversed. S/D ratio of 3 was considered abnormal after 32th weeks of pregnancy. CPI ≤ 1 was considered abnormal. Special inquiry was made regarding smoking and drug use, and previous antenatal check-ups were noted. On admission, a complete history of present complaints, obstetric history, menstrual history, past medical and surgical history, and family history were taken. General physical examination was done to assess both maternal and fetal conditions. Abdominal examination and per vaginal examination were done. Blood samples for complete blood count, RBS, urine R/M, and viral markers were sent. After delivery, cord blood was drained, and placentas were collected and fixed with 10% formalin. Shape of placenta, weight in grams, size, diameter in centimeters, and deposition were examined. Fetomaternal outcome was also note the investigation was started after receiving ethical approval from the hospital. Written informed consent was obtained from all the study subjects.

Statistical analysis

The data were collected and tabulated with the help of collected and tabulated with the help of appropriate software. Continuous data were represented as mean and standard deviation and were analyzed by one-way analysis of variance. Frequency variables were presented as number and percentage and were analyzed by Chi-square tests.

Observation & Result

Table 1: Baseline characteristics of study subjects

Age group	Number	Percentage
≤20 years	10	10
21-30 years	78	78
31-40	9	9
>40	3	3
Booking status		
Booked in institution	37	37
Unbooked	63	63
Gravida		
G1	61	61
G2	24	24
G3	13	13
G4	2	2

Table 2: Fetal outcome among study subjects

Live birth or stillbirth	Number (n = 100)	Percentage
Live birth	95	95
IUFD	5	5
Weight (in kg) mean (SD)	1.98	0.44
APGAR score	At 1 min	At 5 mins
Critically low	0	1
Below normal(4-6)	44	16
Excellent (7-10)	54	79
NICU admission		
Signs of fetal distress	66	66
NICU admission present	65	65
Outcome		
Discharged	82	82
Expired	14	14
Intrauterine fetal death	4	4

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Table 3: Value of uterine artery Doppler in predicting pre-eclampsia

Doppler test	True positive	False negative	False positive	True negative	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Uterine artery								
S/D	3	2	6	89	60	93.7	33.3	97.3
RI	2	3	6	89	40	96.7	25	96.7
Notch	3	2	5	90	60	97.7	37.5	97.8
Combined	4	1	10	85	80	89.4	18.6	98.8

Discussion

Highest number of cases were in the age group of 21–30 years, with a mean age of 26.24±4.56 (range: 18–44 years). Only 37% of females were booked, and 66% of cases belonged to G1. Maximum cases were of Mild Pre eclampsia (43%) followed by gestational hypertension (29%), Severe Pre eclampsia (20%) and 9 cases of eclampsia.

Maternal complications due to PIH were noted, like eclampsia (9 cases), HELLP syndrome (5 cases), PRES (Posterior Reversible cerebral Encephalopathy Syndrome, 2 cases), pulmonary edema (2 cases).

Although cases of placental infarction were higher in neonatal intensive care unit (NICU) admitted cases as compared to non-admitted cases (61.33% vs. 45.42%, respectively), calcification was higher in NICU-admitting cases as compared to non-admitting cases (95.76% vs. 84.3 vs. 5.11%, respectively). Syncytial knots were higher in neonatal intensive care unit (NICU) admitted cases as compared to non-admitted cases 93.78% vs 81.47%, also grade fibrosis was 45.12% vs. 27.12%, Fibrinoid necrosis (70.43% vs. 54.49%) and leukocytic infiltration (68.28% vs. 64.16%) respectively. Statistically, no significant difference was observed in all parameters.

The mean systolic blood pressure and diastolic blood pressure was 166.28±14.88 mmHg and 105.24±8.90 mmHg, respectively. We have found that 98.6% of cases had pedal edema and only 2 cases had pallor. On ultrasonography, 52.4% of placenta belonged to Grade III and 47.6% of cases belonged to Grade II. The mean diameter in cm, biparietal diameter (mm), weight (g), number of cord vessels and Cord length (cm) was 17.59±1.87 cm, 411.22±54.31 g, 3±0.00, 44.65±4.23 cm, respectively. On histopathological examination of placenta, 92% of cases belonged to calcification, followed by syncytial knots: 90%, infarction: 56%, grade leukocytic infiltration: 67%, grade fibrinoid necrosis: 66%, infarction:

56%, and grade fibrosis: 52 percent of cases belonged to vaginal delivery and the rest 48% belonged to C-section. 96 percent of cases belonged to live birth and 4% belonged to IUFD. The mean weight (kg) was 1.98±0.44 kg, respectively, with a range of min and max 1–2.6 kg. According to Apgar score, 44% of cases belonged to score 4–5 moderately depressed (below normal) at 1 min, while at 5 min, one case was in critically low condition and 16% of cases belonged to moderately depressed (below normal) condition. 65 percent of babies were admitted to neonatal intensive care unit (NICU) and 66% of cases had signs of fetal distress.

Grade fibrinoid necrosis was observed 66%, also Al-Bakri *et al*. observed that the histological study of placenta with gestational hypertension showed a significant increase in syncytial knots and calcification and hyalinization area also fibrinoid necrosis are observed hypertensive disorders of pregnancy adversely influence the morphology of placenta.

We have found that 82% of cases belonged to discharged, f 14% belonged to expired, and 4% belonged to stillbirth. patients admitted to NICU, out of them, 42% of cases belonged to respiratory distress/low birth weight (LBW) and 20% respiratory distress, 2% of cases were only LBW and only one case was observed with hydronephrosis/LBW. Histological changes of placenta from the hypertensive mothers also showed a 92% significant increase in calcification, perivillous fibrin deposition also in Samaddar *et al*. [10] study, 44% of the placentas in the hypertensive group showed evidence of calcification.

In the present study, according to mode of delivery, where we have found that 52% of cases belonged to vaginal and the rest 48% of cases belonged to C-section. Similar to the present study, preterm deliveries were high in hypertensive groups in the published

Conclusion

Doppler ultrasound offers the ability to screen cases of pregnancy induce hypertension early in gestation with a reproducible non-invasive haemodynamic testing mechanism. Doppler indices from the fetal circulation can reliably predict adverse perinatal outcome in an obstetric patient in high risk population like PIH population. The knowledge of uterine and umbilical artery waveform may help to improve pregnancy management and any permit identification and assessment of pregnancy induced hypertension at earliest gestation age as compared to other antepartum test modalities. Early identification creates possibility of early intervention and therapy. The Doppler patterns follow a longitudinal trend with early changes in the umbilical artery followed by middle cerebral artery and other peripheral arteries. Venous changes follow the arterial pattern and occur in severely compromised fetus. Doppler investigation plays an important role in monitoring the redistributing growth restricted fetus and thereby may help to

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determine the optimal time for delivery. The findings of the present study thus suggest that placental morphology and histopathology are affected in hypertensive pregnancies, which might be the reason for placental insufficiency in these cases. Separate research is needed to determine how these morphological and histopathological changes affect maternal and perinatal outcome needs to be studied separately.

During pregnancy significant histomorphological changes in placenta are caused due to hypertensive disorders which lead to harmful and severe foetal outcomes. The villous lesion in hypertensive placenta like cytotrophoblasts proliferation, proliferation of endothelial lining of capillaries, stromal fibrosis, calcification, hyalinisation of villi and infarction were found to be statistically significant in cases. A valuable insight into the mechanism of placental dysfunction can be achieved through a detailed examination after delivery.

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