



Estimating the Association of Ultrasonographical Placental Grading in Utero to Gestational Age and Feto-maternal outcomes in Hypertensive Disorders of Pregnancy

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Study Protocol

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ABSTRACT

Background: Worldwide, about 5-8% of all pregnant females are affected by hypertensive disorders. In rural India, the incidence is 10%. This entity has become a significant cause of maternal mortality and morbidity, resulting in 10-15% of all maternal fatalities in developing nations, particularly in developing nations. Hence, identifying this entity in pregnant females and its timely management is vital for both mother and baby. Gestational hypertension can cause placental insufficiency due to narrowing and occlusion of uteroplacental vessels leading to intrauterine growth retardation. This study aims to detect placental grading by ultrasonography in the third trimester in cases of hypertensive disorders of pregnancy and to assess its correlation with fetal-maternal outcomes.

Methodology: This will be a cross-sectional study carried out in the Department of Obstetrics and Gynecology, AVBRH, Wardha. About 130 pregnant normotensive females and 130 hypertensive pregnant females will be included in the study. Baseline data such as age, sex, parity, routine laboratory data, PIH profile, sonography scans will be collected. All the patients will be followed till delivery, and feto-maternal outcomes will be assessed. Data will be analyzed with appropriate statistical tests.

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Expected Outcome: A significant correlation is expected between higher placental grading in hypertensive pregnant females compared to normotensive patients and will have a significant association with perinatal and fetal morbidity.

Keywords: *Gestational hypertension; pregnancy; ultrasonography; perinatal; morbidity; mortality; placenta.*

1. INTRODUCTION

Worldwide, about 5-8% of all pregnant females are affected by hypertensive disorders [1]. In rural India, the incidence is 10% [2]. This entity has become a significant cause of maternal mortality, and morbidity resulting in 10-15% [3] of all maternal fatalities in developing nations [4]. Hence, identifying this entity in pregnant females and its timely management is of utmost importance for both mother and baby [5].

The placenta is the most important for fetal prenatal records. It is responsible for the growth and maturation of fetus in utero. Abnormal placental function is a major cause of hypertensive disorders of pregnancy. Placenta in these disorders tends to be smaller in size and mature earlier in comparison to normal pregnancy. Placental changes in hypertensive disorders reflect fetal growth retardation, low birth weight fetus, prematurity, and sometimes stillbirth, resulting in adverse perinatal outcomes. The main cause of reduction in fetoplacental blood flow in hypertensive disorders in pregnancy is the failure of trophoblastic invasion, which usually occurs around the 16th week of gestation [6].

Extravillous cytotrophoblasts are fetally derived cells that arise from villi and come in contact with maternal decidua to encounter maternal immune cells. These tumor-like cells are responsible for invading myometrium of the uterus and upto spiral arteries leading to formation of large vessels with low resistance. The invasion results in the loss of musculo-elastic structure of arteries and conversion into fibrinoid like material, which contains trophoblastic cells inside it. This physiological transformation of endovascular invasion occurs in two stages; first into decidual part of spiral arteries at 8-10 wks and second into myometrium at 16-18 wks. These changes are responsible for normal pregnancy.

In hypertensive disorders in pregnancy; cytotrophoblast fail to express PECAM-1 molecule. There is evidence that these PECAM-1 molecules express endothelial cell adhesion

molecules responsible for trophoblastic invasion. Thus in hypertensive disorders; trophoblast is less invasive into spiral arteries and shows more proliferation, which leads to a gradual rise in utero placental resistance and reduced blood flow to fetus. Thus endothelial dysfunction in hypertensive disorder of pregnancy is responsible for uteroplacental insufficiency and fetal growth retardation leading to compromised maternal and fetal outcome [6].

The National High Blood Pressure Education Program Working Group classified hypertensive disorders of pregnancy into 4 groups:

1.1 Chronic Hypertension

Blood pressure > 140/90 before 20 weeks of gestation and not associated with any trophoblastic disorders of pregnancy and without significant proteinuria (<30 mg/ml or < 300mg/day) or hypertension first diagnosed after 20 wks of gestation and BP persistently raised after 12 weeks post partum.

1.2 Pre-Eclampsia-Eclampsia

Pre Eclampsia: Bp > 140/90 diagnosed after 20 wks of gestation with significant proteinuria (0.3g/dl urine i.e. > +1 on dipstick or > 30mg/ml urine or > 300mg/day).

Eclampsia: Pre eclampsia with seizures which any other cause cannot explain.

1.3 Pre-eclampsia Superimposed on Chronic Hypertension

Previous hypertensive with new onset proteinuria > 300 mg/day diagnosed after 20 wks of pregnancy or sudden increase of blood pressure or proteinuria or decrease in platelet count less than 1 lac/mm³ in previously hypertensive women with proteinuria before 20 wks of gestation.

1.4 Gestational Hypertension

Blood pressure > 140/90 mm hg recorded for first time in pregnancy not associated with proteinuria

and which returns to normal within 12 wks postpartum [5].

Hypertension in pregnancy causes placental insufficiency, which leads to decrease in fetal growth leading to IUGR. Decrease in utero-placental blood flow due to narrowing and occlusion of utero placental vessels in hypertensive disorders leads to various histological as well as ultra structural changes in hypertensive placentas [7]. This specific micro and macroscopic placental changes leads to various complications in pregnancy and is associated with increased perinatal morbidity and mortality [8].

Ultrasound is used to visualize these specific changes in placenta which signifies placental maturity. Physiologically, placental ageing occurs due to calcium deposition throughout pregnancy. Placental grade signifies the quantity of calcium deposited. The calcium deposition is microscopic in the first 2/3rd of gestation. After 33 weeks, more than half of placentas show macroscopic calcifications which continues to increase till term. Sonographically these calcium deposits appear as echogenic foci.

In order to categorize maturation of placenta; a method was described by Grannum 7 and his associates to classify and grade placenta by ultrasonic evaluations of placental appearance occurring during gestation in vivo placenta. Placental grading will be determined using Grannum grading from 0 to 3 by noting basal plate, chorionic plate, and placental substance.

- Grade 0 - placenta contains delineated straight chorionic plate and a homogenous texture.
- Grade 1 - placenta has an undulating chorionic plate and scattered echogenic areas.
- Grade 2 - small echogenic areas in the placenta along the basal layer, comma like echogenic areas at the chorionic plate.
- Grade 3- echogenic indentations from chorionic plate to basal plate forming discrete cotyledons [9].

The fetal pulmonary maturity derived by L/S ratio was correlated with placental maturation as seen by ultrasound [8]. Grade 3 placenta was found to be 100% correlated between L/S ratio by Petrucha and his associates [10]; whereas Quinlain 9 and Cruz reported 3 cases of grade 3 placenta having immature L/S ratio [11].

Studies outline conflicting views pertaining to grade 3 placenta as observed before 34 weeks of gestation. Several studies suggest that there exists a correlation between early placental maturation and perinatal complications such as pre eclampsia, intra uterine growth restriction and non reassuring fetal status. But yet certain studies disagree that advanced placental grade is associated with fetal maturation [12]. Therefore this study has been done to detect placental grading by ultrasonography in third trimester in hypertensive disorders of pregnancy and correlate it with fetal and maternal outcome.

2. BACKGROUND/RATIONALE

This study is to understand about placental maturity in hypertensive disorders of pregnancy and normal pregnancy and to correlate it with fetal outcome so as to give appropriate and timely management to reduce perinatal morbidity and mortality.

2.1 Aim

To study the association of ultrasonographically observed placental grading in utero to gestational age and to evaluate its importance with respect to foeto maternal outcome in hypertensive disorders of pregnancy.

2.2 Objectives

- 1) Detecting sonographic placental grading in hypertensive disorders of pregnancy and normotensive patients.
- 2) To compare the placental grading in hypertensive disorder of pregnancy and normotensives.
- 3) To know mode of delivery.
- 4) To compare fetal outcome in terms of APGAR score at 1 and 5 mins and NICU admission in both hypertensive disorders in pregnancy with normotensives.

3. METHODS

Duration of Study: September 2020 to September 2022.

Place of Study: Department of Obstetrics and Gynaecology, DMIMS (Deemed to be University, Wardha.)

Study Design: Prospective Observational Study.

Sample Size: 130 patients in each group will be calculated by using the following formulae:

$$n = \frac{(Z_a + Z_b)^2 [P_1(1-p_1) + P_2(1-P_2)]}{(P_1 - P_2)^2}$$

Where,

Z_a is the level of significance at 5% i.e 95%

Confidence interval= 1.96

Z_b= Power of the test = 80% =0.84

P₁= Proportion of placental grade in control group = 33% = 0.33

P₂= Proportion of placental grade in study group = 18% = 0.18

$$n = \frac{(1.96 + 0.84)^2 [0.33(1-0.33) + 0.18(1-0.18)]}{(0.33-0.18)^2}$$

$$= 128.47$$

$$= 130 \text{ Patients needed in each group}$$

In this study, 130 participants for each group will be taken after ethical clearance from the institutional ethical committee. Before enrolling the patient into the study, every woman will be explained the type and nature of the study and informed consent will be taken.

Study group A- 130 Pregnant patients with hypertensive disorders of pregnancy fulfilling the inclusion criteria will be included.

Study group B- 130 pregnant females who are normotensive and matching in age, parity and gestational age and fulfilling the inclusion criteria will be included.

3.1 Inclusion Criteria

3.1.1 Study group

- 1) Pregnant women after 28 weeks of gestation willing to participate in study.
- 2) Bp > 140/90 mm hg
- 3) Vertex presentation
- 4) no other medical disorders like diabetes, renal disease, thyroid
- 5) singleton pregnancy.

3.1.2 Control group

- 1) Pregnant women after 28 weeks of gestation willing to participate in study.
- 2) Bp < 140/90 mm hg
- 3) Vertex presentation
- 4) No other medical disorders like diabetes, renal disease, thyroid

- 5) Singleton pregnancy.

3.2 Exclusion Criteria

3.2.1 Study group

1. Diabetes
2. Thyroid disorders
3. Cardio vascular disorders
4. Renal diseases
5. Pregnancy associated with other medical disorders
6. Twins
7. Patients not willing to participate

3.2.2 Control group

1. Hypertension
2. Diabetes
3. Thyroid disorders
4. Cardio vascular disorders
5. Pregnancy associated with other medical disorders
6. Twins
7. Patients not willing to participate

4. METHODOLOGY

Study will be conducted in department of obstetrics and gynecology in AVBRH, Sawangi Meghe Wardha. This study will be conducted for a period of two years . Data for the study will be collected from 130 hypertensive disorder of pregnancy (Group A) and 130 normotensive (Group B) patients attending the Department of Obstetrics and Gynecology in ACHARYA VINOBA BHAVE RURAL HOSPITAL attached to DATTA MEGHE MEDICAL COLLEGE, SAWANGI MEGHE.. They will be included after meeting inclusion and exclusion criteria and informed valid consent will be taken of all the participants. Study group (A) and control group (B) will be subdivided on gestational age into two groups:

1. from 28 to 34 weeks of gestational age
2. from 34 to 40 weeks of gestational age

Control group will be matched in age, parity and gestational age. Detailed history will be taken and general, systemic and obstetric examination will be done of all the patients. Routine blood tests will be done of all the patients including sonography. Study group patients (Group A) will be further investigated for Urine albumin levels, APTT INR serum uric acid and serum LDH levels and funduscopy. All patients will be advised

ultrasound examination after 28 weeks of gestation and all sonography parameters (like amniotic fluid index, gestational age and expected weight) will be measured. Placental grading will be done as per the basis of Grannum scale(8) . Placental grading will be noted for group A sub groups and B sub group patients .Patients will be followed till delivery; the outcome of group A subgroups and B subgroups will be studied in terms of placental grading and its relation to fetal outcome in terms of Apgar score at 1 and 5 mins and NICU admissions and maternal outcome in terms of mode of delivery. We shall be applying for funding from intramural grant/ ICMR grant/ concession for synopsis.

5. RESULTS

Primary outcome: Comparing placental grading by ultrasonography between hypertensive disorder of pregnancy and normotensive pregnant patients.

The study will include 130 pregnant patients with hypertensive disorders of pregnancy (Group A) and 130 normotensive patients (Group B). Both the groups will be further divided into two subgroups on the basis of gestational age, first group between 28 to 34 weeks and second between 34 to 40 weeks. The ultrasonic placental gradings will be done for both the subgroups for both control and study group and comparison will be made. Secondary outcomes like outcome of pregnancy and neonatal wellbeing will also be assessed. The desired outcome in this study is to understand early placental maturity in hypertensive pregnant females with comparison to normal pregnancy and to correlate it with fetal outcome so as to give appropriate and timely management to patients with hypertensive disorders of pregnancy to reduce perinatal morbidity and mortality.

6. DISCUSSION

5-8% of all pregnant women, worldwide are affected by hypertensive disorders of pregnancy. Hypertensive disorders in pregnancy are related to adverse maternal and perinatal outcomes. This disorders are associated with placental insufficiency, leading to decrease blood flow to fetus resulting in decrease in fetal growth, thus causing IUGR. Hence identifying this entity is of utmost importance. Reduced uteroplacental flow has been recognized in such patients, this reduction of blood flow is due to early placental maturation due to micro and macroscopic

changes in placenta. Ultrasound thus plays a vital role in early detection of these placental changes. With increase in gestational age, changes in placenta detected by ultrasound have been reported first by Weinsberg et al but placental gradings were given by Grannum et al. [8].

One such study taken up among third trimester pregnant hypertensives concluded increased fetal complications with hypertensive females whereas increased placental grading were not related to adverse perinatal outcome. Whereas another study taken up to detect placental maturity in hypertensives and its effect on fetal outcome proved that hypertensives had increased placental maturity and compromised fetal outcome in comparison to normotensives with less placental maturity [13].

The problems of eclampsia is evident from many GBD studies [14-16]. Few studies related to pregnancy and ultrasonography were reviewed [17-20]. Studies done in Institute of medical lab technology showed that grade 2 placenta were associated with hypertensive pregnancies and more incidences of lower abdominal pain. It has thus been proved in many studies that there is accelerated placental maturation in hypertensive pregnant. But it has not been very clearly established that increased placental grading is also associated with adverse perinatal outcome [9]. Nonetheless there have been studies showing grade 3 placenta when present in early third trimester leads to decrease in uteroplacental circulation resulting in compromised fetal outcome. This was commonly seen in patients with hypertension, APH and IUGR cases. And hence women with accelerated placental maturity specially in early third trimester should be an alerting factor for obstetrician to look for risk factors. And thus, pregnant females with increased placental grade should be followed up by ultrasound to closely monitor and manage appropriately. This study has been undertaken to correlate hypertensive disorders with increasing placental maturation and its fetal and maternal outcome [21-26].

7. CONCLUSION

Hypertensive disorders in pregnancy affect about 5-8% of all pregnant females. They are more common in developing countries. They are one of the leading factors leading to compromised maternal and fetal outcome. Hence it becomes important to identify this entity early in pregnancy and manage accordingly. Hypertension is

associated with accelerated placental maturity. When placenta matures early in pregnancy, it results into uteroplacental insufficiency leading to decreased blood flow to fetus which can further lead to IUGR, fetal hypoxia and increased perinatal complications. It can also result into adverse pregnancy outcome, and hence we have designed this study in order to follow up pregnant females and their sonographic placental grade and correlate it with fetal and maternal outcome so as to understand effects of hypertension on placental maturity and its correlation with fetal and maternal complications.

ETHICAL APPROVAL AND CONSENT

In this study, 130 participants for each group will be taken after ethical clearance from the institutional ethical committee. Before enrolling the patient into the study, every woman will be explained the type and nature of the study and informed consent will be taken.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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