UTERINE ARTERY DOPPLER IN FIRST TRIMESTER (11-13+6WKS) IN PREDICTION OF ADVERSE PREGNANCY OUTCOME

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In fulfilment of the requirements for the award of the degree of

M.S. OBSTETRICS & GYNAECOLOGY

Under the guidance of

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PSG INSTITUTE OF MEDICAL SCIENCES & RESEARCH, COIMBATORE

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI, TAMILNADU

MAY 2018

CERTIFICATE BY THE HOD AND DEAN OF THE INSTITUTION

This is to certify that **Dr.Arivarasi Sai Gokull Raj**, REG NO: 221516451 postgraduate student (2015–2018) in the Department of Obstetrics & Gynaecology, PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH, Coimbatore has done this dissertation titled **"UTERINE ARTERY DOPPLER IN FIRST TRIMESTER (11-13+6WKS) IN PREDICTION OF ADVERSE PREGNANCY OUTCOME"** under the direct guidance and supervision of guide **Prof. Dr.BALASUDHA.K, DGO, DNB(OG)** in partial fulfilment of the regulations laid down by The Tamilnadu Dr. M.G.R. Medical university, Chennai, for the award of M.S., Degree in Obstetrics and Gynaecology

Seal and Signature of the HOD   Seal and Signature the Dean

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CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled, **"Uterine artery Doppler in the first trimester (11-13+6wks) in prediction of adverse pregnancy outcome"** is the bonafide original work of **Dr.Arivarasi Sai Gokull Raj,** done under my direct guidance and supervision in the Department of Obstetrics and Gynaecology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfilment of the regulations by The Tamil Nadu Dr.MGR Medical University, Chennai for the degree of M.S in the department of Obstetrics and Gynaecology.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"UTERINE ARTERY DOPPLER IN FIRST TRIMESTER (11-13+6WKS) IN PREDICTION OF ADVERSE PREGNANCY OUTCOME"** is a bonafide and genuine research work carried out by me in the Department of OBSTETRICS AND GYNAECOLOGY, PSG Institute of Medical Sciences and Research, Coimbatore, under the guidance of **Dr .Balasudha.K, DGO,DNB (OG),** Professor of Obstetrics & Gynaecology. This dissertation is submitted to The Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the university regulations for the award of MS degree (Obstetrics & Gynaecology, Examination to be held in May 2018. This dissertation has not been submitted for award of any other degree or diploma.

Place: Coimbatore

Date: Signature of the Candidate

                                                         Dr. Arivarasi Sai Gokull Raj

CERTIFICATE – II

This is to certify that this dissertation work titled **UTERINE ARTERY DOPPLER IN FIRST TRIMESTER (11-13+6WKS) IN PREDICTION OF ADVERSE PREGNANCY OUTCOME** of the candidate **Dr. ARIVARASI SAI GOKULL RAJ** with registration Number **201516451** for the award of **MASTER IN SURGERY** in the branch of **OBSTETRICS & GYNAECOLOGY**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **0%** of plagiarism in the dissertation.

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INTRODUCTION Pregnancies are complicated by Hypertensive disorders of about 5-10% and along with hemorrhage, sepsis and fetal growth restriction constitutes a triad contributing to maternal morbidity and mortality1,2. Hypertensive disorders in pregnancy vary from mildly elevated blood pressure to severe hypertension with multi organ dysfunction. Of these disorders the preeclampsia syndrome , either alone or superimposed on chronic hypertension and its associated maternal mortality is the most dangerous and it accounts for 16% and is preventable3. The incidence of preeclampsia varies between 8-10% of all pregnancies. In nulliparous woman, the incidence of preeclampsia ranges between 2% and 7% (who conceive with Assisted Reproductive technology).This is responsible for 29,000 maternal deaths per year world wide.4,5 There is 5-fold increase in perinatal mortality in pre-eclampsia due to iatrogenic prematurity, respiratory distress syndrome and neonatal intensive admission 6,7. In India, Incidence of hypertensive disorders in pregnancy is 5.38%,while preeclampsia and eclampsia accounted for 44% and 40% complications respectively.Maternal and perinatal deaths have been reported in 5.5% and 37.5% of deliveries8. Intensive maternal and fetal monitoring in such high risk patients would lead to an earlier diagnosis of the clinical signs of the disease and the associated fetal growth restriction and avoid the development of serious complications such as placental abrupton , eclampsia , Intrauterine death through such interventions as the administration of antihypertensive medication and early delivery. Modern antenatal care provision is focussed on a risk – based approach to monitoring for adverse pregnancy outcomes such as preeclampsia ,fetal growth restriction, placental abruption, still birth and pregnancy outcome of baby. Early identification of the high-risk group for the development of adverse pregnancy outcome is also important for future studies investigating the potential role of pharmacological interventions starting from the first trimester to improve placentation and reduce the prevalence of the disease. Several prophylactic therapies (anti-oxidant, vitamins, folic acid supplementation and aspirin) have so far tried to prove its efficacy in the prevention of preeclampsia in healthy nulliparous groups. The term Gestational Hypertension used now to describe any form of new onset pregnancy related hypertension. Antenatal outcome can be improved by early identification of pre-eclampsia by alerting the clinicians to the need of therapeutic prophylaxis and additional surveillance later in pregnancy, thus an increase in perinatal surveillance with significant decline in maternal and fetal mortality and morbidity which is associated with pre-eclampsia and eclampsia. Impaired placentation with abnormal blood flow velocity and resistence in placental vessels is associated with pre-eclampsia and fetal growth restriction. Prediction of hypertensive disorders and associated adverse outcomes by Ultrasonography plays an important role. Uterine artery Doppler waveform analysis has been extremely studied in the second trimester of pregnancy as a

CONTENTS

INTRODUCTION

Pregnancies are complicated by Hypertensive disorders of about 5-10% and along with hemorrhage, sepsis and fetal growth restriction constitutes a triad contributing to maternal morbidity and mortality[1,2]. Hypertensive disorders in pregnancy vary from mildly elevated blood pressure to severe hypertension with multi organ dysfunction. Of these disorders the preeclampsia syndrome , either alone or superimposed on chronic hypertension and its associated maternal mortality is the most dangerous and it accounts for 16% and is preventable[3].

The incidence of preeclampsia varies between 8-10% of all pregnancies. In nulliparous woman, the incidence of preeclampsia ranges between 2% and 7% (who conceive with Assisted Reproductive technology).This is responsible for 29,000 maternal deaths per year world wide.[4,5]

There is 5-fold increase in perinatal mortality in pre-eclampsia due to iatrogenic prematurity, respiratory distress syndrome and neonatal intensive admission [6,7].

In India, Incidence of hypertensive disorders in pregnancy is 5.38%,while preeclampsia and eclampsia accounted for 44% and 40% complications respectively.Maternal and perinatal deaths have been reported in 5.5% and 37.5% of deliveries[8].

Intensive maternal and fetal monitoring in such high risk patients would lead to an earlier diagnosis of the clinical signs of the disease and the associated fetal growth restriction and avoid the development of serious complications such as placental abrupton , eclampsia , Intrauterine death through such interventions as the administration of antihypertensive medication and early delivery. Modern antenatal care provision is focussed on a risk – based approach to monitoring for adverse pregnancy outcomes such as preeclampsia ,fetal growth restriction, placental abruption, still birth and pregnancy outcome of baby. Early identification of the high-risk group

for the development of adverse pregnancy outcome is also important for future studies investigating the potential role of pharmacological interventions starting from the first trimester to improve placentation and reduce the prevalence of the disease. Several prophylactic therapies (anti-oxidant, vitamins, folic acid supplementation and aspirin) have so far tried to prove its efficacy in the prevention of preeclampsia in healthy nulliparous groups.

The term Gestational Hypertension used now to describe any form of new onset pregnancy related hypertension.

Antenatal outcome can be improved by early identification of pre-eclampsia by alerting the clinicians to the need of therapeutic prophylaxis and additional surveillance later in pregnancy, thus an increase in perinatal surveillance with significant decline in maternal and fetal mortality and morbidity which is associated with pre-eclampsia and eclampsia.

Impaired placentation with abnormal blood flow velocity and resistence in placental vessels is associated with pre-eclampsia and fetal growth restriction. Prediction of hypertensive disorders and associated adverse outcomes by Ultrasonography plays an important role.

 Uterine artery Doppler waveform analysis has been extremely studied in the second trimester of pregnancy as a predictive marker for the late development of pre eclampsia and fetal growth restriction. The use of Doppler interrogation of this vessel in the first trimester has gained momentum in recent years. In normal pregnancy ,the feto placental circulation acts as a low resistance system unit. Thus blood velocity waveforms in umbilical artery show continuos forward flow throughout the cardiac cycle. Impaired placental perfusion ,one of the hallmarks of preeclampsia, can be assessed by measuring flow waveforms ratios or by detecting diastolic notching of the uterine and umbilical vessels. According to the National Institute for Clinical

Excellence guidelines on routine prenatal care recommending that at the first prenatal visit a woman's level of risk for adverse pregnancy outcome should be evaluated so that a plan for her schedule of prenatal visits can be formulated. There is no proven effective method for the prevention of PE.

Currently there is no treatment which can prevent all cases of preeclampsia, there is evidence that low dose aspirin started early in pregnancy have some role in reducing the incidence of adverse pregnancy outcome in significant no of cases now.. Prophylactic aspirin reduces early on PE and preterm delivery by 10%.[9]

AIM AND OBJECTIVE

Aim:

- The aim of the study is to evaluate the first trimester uterine artery Doppler in the prediction of the development of adverse pregnancy outcome.

Objectives:

- Correlation of uterine artery Doppler in the first trimester with adverse pregnancy outcome.

MATERIALS AND METHODS

Source of Data

This is a prospective screening study for women attending antenatal clinic during 11-13 weeks + 6 days of gestation in PSG IMSR, Coimbatore. In this visit, women will have an ultrasonogram for the following reasons:

(1) to confirm gestational age from the measurement of the fetal crown-rump length (CRL)

(2) to diagnose any major fetal abnormalities

(3) to measure fetal nuchal translucency thickness and nasal bone, as part of the screening for chromosomal abnormalities.

(4) Along with this Informed consent will be obtained and Uterine artery Doppler Pulsatile Index(PI) will be measured by Transabdominal or Transvaginal colour Doppler.

Methodology of the study:

Study Design: Prospective longitudinal Observational study.

Sample size: 150 no's (Control – 75 and case group – 75)

All women meeting inclusion criteria during jan 2016 – jan 2017

- **With Reference Study** : Evaluating the optimal definition of abnormal First – Trimester. Uterine Artery Doppler Parameters to Predict Adverse Pregnancy Outcomes.

  [From - J Ultrasound Med. 2015 jul ;34(7);1265-9,doi;10.7863/ultra.34.7.1265]

Calculation:

n = 4 x p x q / d2

P = 45

Q = 100 – p

100-45 = 55

d = precision (20% of 45)

d = 20 x 45 / 100

d = 9

n = 4 x 45 x 55/ 9 x 9

n = 122 (calculated sample)

Place: Department of Obstetrics and Gynaecology – OPD

PSG Institute of Medical Science and Research Centre, Peelamedu , Coimbatore

Duration: 1 Year , 1ˢᵗ Jan 2016 – 1ˢᵗ Jan 2017

Method: This is a Hospital based prospective study.

Inclusion Criteria

- All pregnant women attending antenatal check up in PSG IMSR

- Between 11 - <13wks + 6 days will be included.

Exclusion Criteria

- Past history of preeclampsia

- Chronic hypertension

- Twins

- Missed abortion

- Major Fetal anomaly which are incompatible with life

- Not consenting.

REVIEW OF LITERATURE

Hypertensive disorders of pregnancy are the most common medical complication in pregnancy with high incidence of maternal and perinatal morbidity and mortality.

DEFINITION OF HYPERTENSION:

Currently, the following thresholds used by NHBPEP and the ACOG to define hypertension is used by most of the international organizations and national bodies.[10,11]

Hypertension is defined as,

- Systolic blood pressure of >/= 140 mmHg and or

  Diastolic Blood pressure >/=90 mmHg (korotkoff 5), on at least two occasions, four to six hours apart within a one week period maximum.

  Diastolic pressure is determined by disappearance of sound(koratokoff phase 5).

- Elevation of > 30mmHg of systolic or more than 15mmHg of diastolic, even the absolute values are <140/90 mmHg is no longer recommended as a criteria (because no evidence to justify that these women have increased risk of adverse pregnancy outcome).[12]

- Blood pressure should be measured by appropriate cuff size (cuff should encircle 80% or more of the arm and cover 2/3rd of the length of the arm)

- Correct positioning of the patient is important in BP assesement, Patient should be seated resting for 5 mins, with the arm at the level of chest,legs not crossing and not talking.

DELTA HYPERTENSION – CONCEPT

A sudden rise in mean arterial pressure (MAP) later in pregnancy even if blood pressure is <140/90 mm of hg is known as "delta hypertension". This is the reason for eclamptic seizures, while women is still considered as normotensive, so close surveillance is needed.

Figure 1: Delta hypertension graphical representation
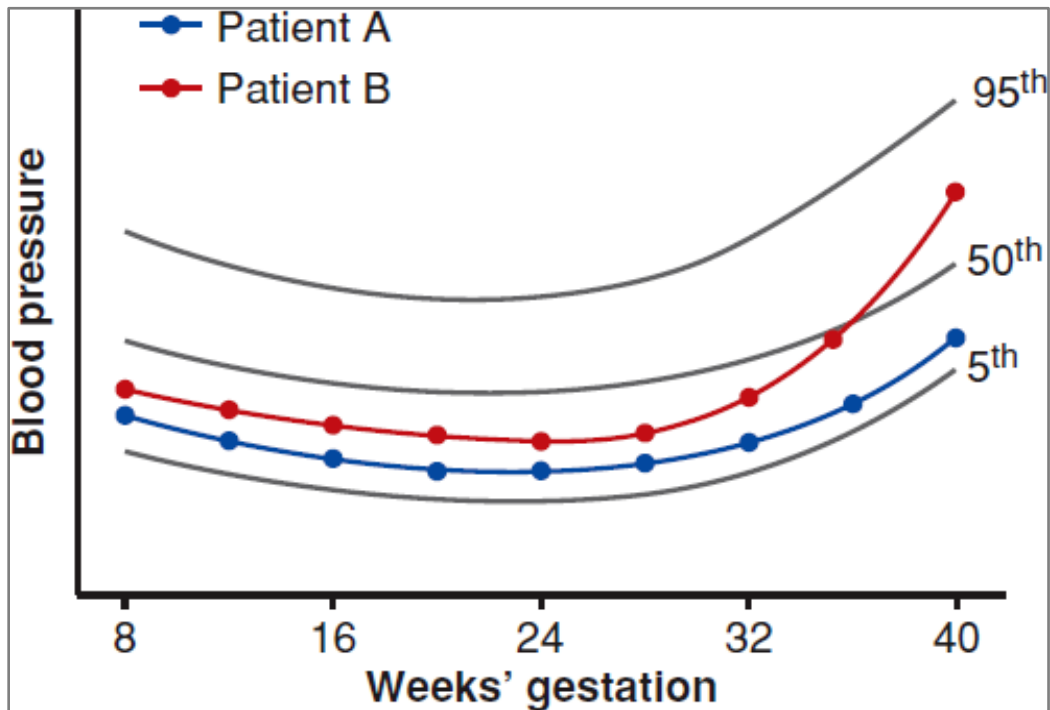
Patient A has BP near 20th percentile throughout pregnancy .

Patient B has a similar pattern till 32 weeks but then begins to increase.

Even though she is at 75th percentile but still considered normotensive.

CLASSIFICATION OF HYPERTENSIVE DISORDERS OF PREGNANCY

Based on International society for the study of Hypertension in Pregnancy (ISSHP), hypertensive disorders in pregnancy is classified into following types

1. Gestational hypertension

2. Pre-eclampsia (PE)

3. Eclampsia syndrome

4. Chronic hypertension – Essential / Secondary

5. Pre-eclampsia superimposed on chronic hypertension

DIAGNOSTIC CRITERIA OF HYPERTENSIVE DISORDERS COMPLICATING PREGNANCY:

1. **GESTATIONAL HYPERTENSION**

   - BP > 140/90 after 20 weeks in a previously normotensive patient on two successive measurement four to six hours apart.

   - Proteinuria - Absent

   - BP returns to normal < 12 weeks postpartum (within 3 months)

   - Final diagnosis made only postpartum

   - May have other signs or symptoms of preeclampsia like epigastric discomfort or thrombocytopenia.

Most common hypertensive disorders of pregnancy with prevalence of 6-15% in nulliparous and 2-4% in multiparous[14]. It is previously known as '"Pregnancy Induced Hypertension"[15]. It can be mild or severe (if BP > 160/110 mmHg).There is higher incidence of

preterm birth and small for gestational age newborns for severe gestational hypertension than mild ones[16].

2. PREECLAMPSIA

Hypertension with associated proteinuria > 0.3g/l in a 24 hour urine collection or 1+ by qualitative urine examination, after 20 weeks of gestation.It is precursor for potentially lethal and severe disease(eclampsia) on its own.Over the several years,"the treatment "is delivery.

Definition – New onset hypertension with BP >/=140/90 mm of Hg with new onset proteinuria after 20weeks in a previously normotensive patient.

Note – Edema is been removed from the definition, because it is too common a clinical finding during pregnancy to be clinically significant.

ACOG (2013)-released guidelines for diagnostic criteria for PE.

➤ Mild PE is defined as "PE without severe features"

➤ Severe PE is defined as "PE with severe features"

➤ Proteinuria (>5gm) has been eliminated from the list of features defining severe features, due to lack of evidence that quantity of protein is associated with significant change in outcome.In its absence PE also be defined as new-onset hypertension with other signs of multisystem involvement.

➤ FGR is removed from the list of features defining severe disease, as guidelines state that management of FGR is the same regardless of diagnosis of PE.

➤ Based on the period of onset, PE is classified into early-onset and late-onset.Early onset PE is defined as development of PE before 34 weeks of gestation,which affects 1% of

population.[18].Late onset is defined as development of PE after 34 weeks of gestation .As compared to late onset PE, early onset is associated with increased maternal mortality and adverse perinatal outcome such as fetal growth restriction, intensive care, preterm care.[19]

A. Mild preeclampsia

✓ BP >/=140/90 mmHg after 20 weeks gestation. Systolic BP < 160 mmHg and diastolic BP< 110 mmHg on two successive measurements four to six hours apart

✓ Proteinuria: Present (>0.3gram in 24 hour sample or 1 + or greater in a random sample, 30mg/dl)

✓ No symptoms, signs or laboratory features of severe preeclampsia

B. Severe preeclampsia

✓ BP >/= 160/110 mmHg

✓ Proteinuria: None to present (> 5 gram in a 24 hour sample or >3 + on two random urine samples collected atleast 4 hours apart)

✓ Headache: Present

✓ Visual disturbances: Present

✓ Upper abdominal pain: Present

✓ Oliguria: Present

✓ Convulsions: Present

✓ Serum creatinine: Elevated

✓ Thrombocytopenia: Present

✓ Serum transaminase level : Marked

✓ Fetal growth restriction: Present

✓ Pulmonary edema: Present

Table 1 – Severity of PE Classification

Criteria	Mild preeclampsia	Severe preeclampsia
Blood pressure	< 160/110	≥ 160/110
Symptoms	Absent	Present
Proteinuria	< 5 g/dl 24 hours collection	> 5 g/dl; ≥ 2+ on dipstick
Liver and Renal function	Normal	Abnormal
Platelet count	Normal	Thrombocytopenia
Pulmonary edema	Absent	Present
Convulsions	Absent	Present
HELLP syndrome	Absent	Present
Fetal growth restriction	Absent	Present

The presence of **any one of the above findings** is sufficient to lead to a classification of the preeclampsia into the severe category

3. ECLAMPSIA

Seizures that cannot be attributed to other causes in a woman with pre eclampsia. It is a severe form of PE. Characterized by sudden onset of generalised tonic- clonic convulsion or coma in pregnancy or postpartum which is unrelated to other cerebral conditions. Based on the time of convulsions, it is designated as antepartum (38-53%), intrapartum(15-21%) and postpartum(11-44%) eclampsia.[20]

4. CHRONIC HYPERTENSION

- BP>/= 140/90 before pregnancy or diagnosed before 20 weeks gestation not attributable to gestational trophoblastic disease.

- Hypertension first diagnosed before 20 weeks gestation and persistent after 12 weeks postpartum

- Proteinuria – absent.

- It complicates 0.5 to 3% of all pregnancies. It can be essential (90%) or secondary (10%)hypertension.

TABLE 2 – CAUSES OF CHRONIC HYPERTENSION

1.Primary or essential hypertension

2.Secondary hypertension
 	
    ➢ Endocrine
 	
        - Diabetes with vascular involvement
 	
        - Hyperthyroidism
 	
        - Congenital adrenal hyperplasia-Primary Aldosteronism
 	
        - Cushing Syndrome
 	
    ➢ Tumours
 	
        - Neuro blastoma
 	
        - Pheochromocytoma
 	
        - wilson's tumour
 	
    ➢ Renal
 	
        - Renal artery Stenosis
 	
        -Renal parenchymal disease (Adult polycystic disease, Reflex nephropathy, Glomerulonephritis)
 	
    ➢ Collagen vascular disease
 	
        - Scleroderma
 	
        - Systemic Lupus erythematosis
 	
    ➢ Heart
 	
        -Coarctation of aorta

.

5. SUPERIMPOSED PRE-ECLAMPSIA [10]

- New onset proteinuria defined as the urinary excretion of 0.3 grams protein or greater in a 24 hour specimen in women with hypertension but no proteinuria before 20 weeks gestation.

- Development of imminent symptoms or platelet count < 100,000 and abnormal liver enzymes.

- About 30% of pregnant women with chronic hypertension develop PE.It usually manifest in early pregnancy than pure PE and is more severe.

ATYPICAL PREECLAMPSIA:

In some woman, preeclampsia and even eclampsia may develop in the absence of either hypertension or proteinuria. TABLE 3 – Criteria for Atypical PE

CRITERIA FOR ATYPICAL PREECLAMPSIA

- ➢ Gestational hypertension plus one or more of the following

    - o Symptoms of preeclampsia

    - o Hemolysis
    - o Thrombocytopenia(< 100,000/ cu.mm)
    - o Elevated liver enzymes: Two times the upper limit of the normal value for Aspartate transaminase (AST) and Alanine transaminase (ALT)

- ➢ Gestational proteinuria plus one or more of the following
    - o Symptoms of preeclampsia
    - o Hemolysis
    - o Thrombocytopenia
- ➢ Early signs and symptoms of preeclampsia-eclampsia at <20 weeks
- ➢ Late postpartum preeclampsia-eclampsia (>48 hours postpartum)

ETIOPATHOGENESIS OF PRE-ECLAMPSIA

Gestational hypertension is more likely to develop in a woman with the following Risk Factors

> Women are at increased risk for PE if they have 1 high risk factor or more than 1 moderate risk factor for PE.

High Risk Factors:

❖ Type 1 or Type 2 diabetes [26]

❖ Chronic hypertension[26]

❖ Chronic kidney disease[26]

❖ Auto immunse disease-APLE/SLE[26]

❖ Hypertension in previous pregnancy[25]

Moderate Risk Factors:

• First time exposure to chorionic villi – first pregnancy.

Chorionic villi is essential need not to be intra uterine.[25]

• Age - >40yrs or more[25] / < 20 years.

• Pregnancy interval of > 10years

• Body Mass Index (BMI) of >35kg/m^2 at first visit,

(risk increases for every increase of 5-7kg/m^2 in pre – pregnancy BMI.[21])

• Family history [25,26]

• multiple pregnancy[20]

• Change of new partner

- Partner who fathered a pre-eclamptic pregnancy in another woman

- Pregnancy due to donor insemination

Note – Smoking regulates adrenomedullin expression, which regulates volume homeostasis.

➢ **Hypertensive disorders are more likely to develop in women with following characteristics.**

1) First time exposure to chorionic villi.

2) Those who are exposed to superabundance of chorionic villi, as seen in molar pregnancy or multiple pregnancy.

   Note – fetus is not a requisite for the development of PE.Chorionic villi is need to be intrauterine.

3) Have pre-existing conditions of endothelial cell activation or inflammation such as diabetes or renal or cardiovascular disease

4) Genetically predisposed to hypertension developing during pregnancy[24,25]

ETIOLOGY

The mechanism by which preeclampsia occurs is not clear, and numerous maternal, paternal, and fetal factors have been implicated in its development.This disorder has a potential to involve all organs in the body.

Mechanisms currently considered important are

- Defective placentation

- Placental ischaemia

- Endothelial cell dysfunction

- Immunological maladaptive tolerance between paternal, maternal and fetal tissues

- In normal pregnancy maternal maladaptation to cardiovascular or inflammatory change

- Genetic factors including epigenetic influences and inherited predisposing genes.

- Nutritional factors

ABNORMAL TROPHOBLASTIC INVASION

Normal placental development requires that cytotrophoblastic invasion in to the maternal spiral arterioles. Placenta receives it blood supply from numerous uteroplacental arteries that are developed by the action of migratory interstitial and endovascular trophoblasts into the walls of spiral arterioles(Remodelling). This transforms the uteroplacental arterial bed into a large capacitance ,low- resistance, low-pressure, high-flow system. This spiral arterioles remodelling starts in the late first trimester and ends by 18- 20 weeks of gestation resulting in replacement of the endothelium and the muscular tunica media. The veins are invaded only superficially. Thus PE has been hypothesized as a "two stage disorder".

FIGURE 2 – Abnormal Trophoblastic Invasion and Outcome
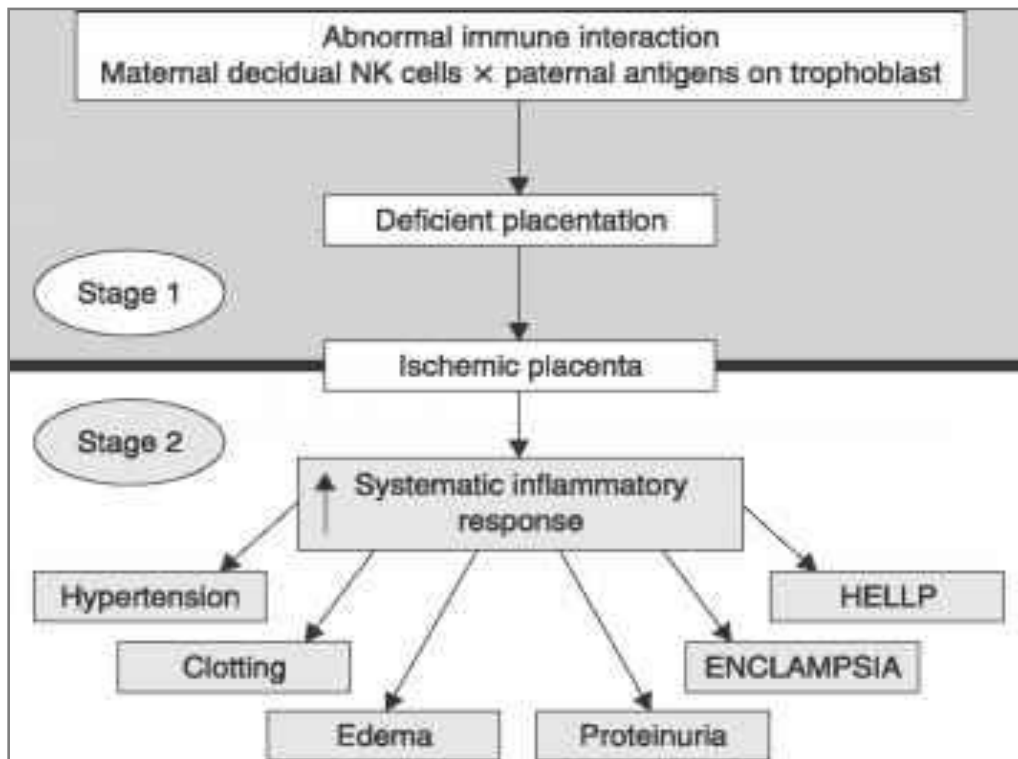
In pre-eclampsia there is incomplete trophoblastic invasion. Here the decidual vessels, but not the myometrial vessels, become lined with endovascular trophoblasts. The deeper myometrial arterioles do not lose the endothelial lining and musculoelastic tissue and their mean external diameter is only half that of corresponding vessel in the normal placenta. This restriction of normal physiological changes leads to restricted placental flow,which becomes more critical with adavancing gestation. The vessels affected by atherosis develop aneurysmal dilatation or obstruction of lumen by atherosis may hinder the placental blood flow, which lead to infarcts, patchy necrosis and damage to intracellular synctiotrophobalst . Infact, studies have shown the degree of incomplete trophoblatic invasion of the spiral arteries is directly associated with the severity of pregnancy induced hypertension.[34]

These abnormally narrow spiral arteriolar lumen are likely to impair the placental blood flow. This leads to diminished perfusion and hypoxic environment eventually lead to release of placental debris or microparticles that incite an inflammatory response.

Defective placentation is postulated to further cause susceptible woman to develop gestational hypertension, preeclampsia syndrome, preterm delivery, a growth restricted fetus and/or placental abruption.

FIGURE 3 – Normal and Abnormal Trophoblastic Invasion Of Spiral Arteries
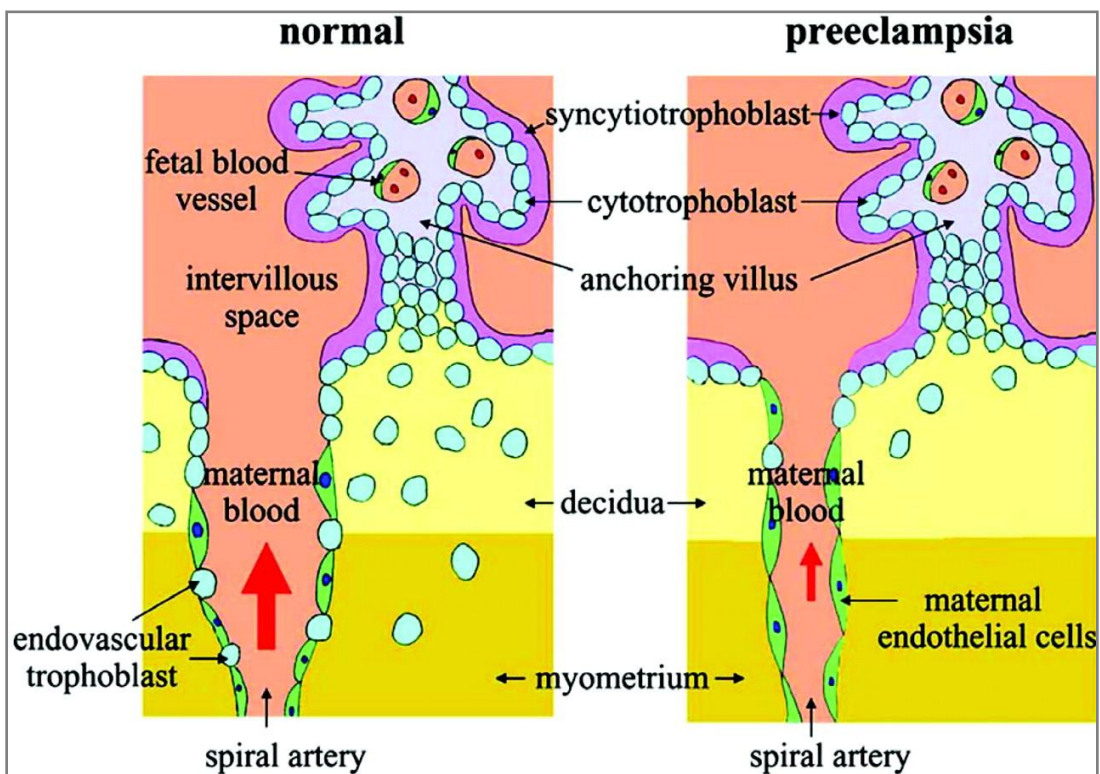
Trophoblastic invasion/differentiation entails changes in the expression of certain cytokines, adhesion molecules, extracellular matrix molecules, metalloproteinase, and class 1b major histocompatibility complex molecule and histocompatibility leucocyte antigen (HLA –G)

Placental implantation with abnormal trophoblastic invasion of uterine vessels leads to myometrial segments of spiral arterioles are left with musculo elastic structure,thereby responsive to hormonal substances.[35]

IMMUNOLOGIC FACTORS

Loss of immune tolerance to paternally derived placental and fetal antigens is another cause accounted for preeclampsia syndrome. Immunological factors may play an important role in the development of pregnancy induced hypertension. This phenomenon in pregnancy induced hypertension include absence of blocking antibodies, decreased cell mediated immune responses, activation of neutrophils and involvement of cytokines. An aberrant immune reaction between fetal trophoblast with maternal tissue in the placental bed is a basic factor in the cause of pregnancy induced hypertension, supported by the findings that this syndrome most often affects first pregnancy. Incidence is also increased by change of partner and in a subsequent pregnancy after birth control methods that prevent sperm exposure. Women who develop pregnancy induced hypertension have decreased proportion of helper T cells (Th 1) in early second trimester, compared with those who remain normotensive. The Th 1/Th 2 imbalance may be mediated by adenosine, found in higher concentration in pregnancy induced hypertension women. The helper lymphocytes secrete cytokines that promote implantation and their dysfunction leads to pregnancy induced hypertension.[37,38]

NUTRITIONAL FACTORS:

In many studies have shown a correlation between dietary deficiencies and the incidence of PE. Diet lack in antioxidants enzymes and antioxidant nutrients, including carotenoids, alpha –tocopherol and thiols are the primary agents against oxidative stress and free radical damage .

These will protect the endothelial cell membrane against free radical produced. When this protective mechanism is lost , the products of lipid peroxidation increase with fall in antioxidant carotenoids. This imbalance leads to oxidative stress and tissue injury.[41,42]

Vitamin C and Vitamin E supplementation between 16 – 22 weeks of gestation decrease the incidence of pregnancy induced hypertension by approximately 50%.[43] In contrast the same supplementation in high risk pregnant women between 14-22weeks gestation with low nutritional status does not prevent PE.[44]

Incidence of preeclampsia was doubled in woman whose daily intake of ascorbic acid was less than 85mg, low dietary calcium intake.

Lycopene is not converted to Vitamin A; hence it may be entirely available for antioxidants. Its supplementation in studies has been shown evidence of decreased incidence of pregnancy induced hypertension and fetal growth restriction by 51.4% and 49.3% respectively.[45]

ENDOTHELIAL CELL ACTIVATION :

Defective placentation leads to an inflammatory state leads to the release of cytokines such as interleukins which may contribute to the oxidative stress associated with preeclampsia.

Other consequences of oxidative stress include production of lipid laden macrophage foam cells seen in atherosis and activation of microvascular coagulation manifest by thrombocytopenia and increased capillary permeability manifest by edema and proteinuria.[36]

GENETIC FACTORS

Familial predisposition for pregnancy induced hypertension has been recognized, single gene model and polygenic inheritance has been suggested. 60% concordance in monozygotic female twin pairs has been reported by a Swedish study. Some have reported a HLA-DR4 association with proteinuria in pregnancy induced hypertension. A number of single gene mutation and inherited thrombophilia's may predispose to pregnancy induced hypertension. Polymorphisms of the genes for Tumour Necrosis Factor, lymphotoxin-alpha and interleukin-1 have been studied with varying results.[39] Genes with possible associations with PE syndrome are mentioned in table 4 .

Table 4 – Genetic Factors Responsible For PE

Gene polymorphism	Function affected
MTHFR(C677T)	Methylene tetrahydrofolate reductase
F5(Leiden)	Factor V_{leiden}
AGT(M235T)	Angiotensinogen
HLA(Various)	Human leukocyte antigens
NOS3(Glu 298 Asp)	Endothelial nitric oxide
F2(G20210A)	Prothrombin(factor II)
ACE(I/D^{at}Intron 16)	Angiotensin-converting enzyme
CTLA4	Cytotoxic T-lymphocyte-associated protein
LPL	Lipoprotein lipase
SERPINE1	Serine peptidase inhibitor

PATHOGENESIS

It is characterised by vasospasm, endothelial cell damage resulting in activation of coagulation system.

1. **Endothelial cell activation** leads to vascular constriction with increased resistance and subsequent hypertension. Decreased blood flow due to mal-distribution and ischemia of the surrounding tissues causes necrosis, hemorrhage and end organ disturbances characteristic of the syndrome.

2. **Vasospasm –**

- **Nitric acid** is a potent vasodilator, synthesized from L-arginine by endothelial cells. It maintains the normal low pressure vasodilated state of feto placental circulation in humans. Damaged or activated endothelial cells produce very less nitric oxide and produce substances that promote coagulation and increase the sensitivity to vasopressin.

- **Increased pressor responses** (Angiotensin 2)

- **Prostaglandins** - Endothelial prostacyclin (PGI2 – a vasodilator) production is decreased in preeclampsia and Thromboxane A2(TXA2 – vasoconstrictor and platelet aggregator) secretion by platelet is increased. This alteration in thromboxane : prostacyclin ratio favours an increased sensitivity to angiotensin ultimately leading to vasoconstriction. If PGI2 > TXA2 ->Vasodilator ->No hypertension. In pregnancy induced hypertension, PGI2 <TXA2 ->Vasoconstriction ->hypertension.[37]

- **Endothelial cell injury** causes decrease in the nitric oxide production.

3. **Endothelins -** Plasma Endothelin -1 levels are increased in normotensive pregnant woman , but woman with preeclampsia have even higher levels. It is produced by human endothelium. These alpha 1-amino acid peptides are potent vasoconstrictors;[46,47]

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4. **Circulating angiogenic factors** - Imbalance between the Angiogenic and Anti-angiogenic factors. Trophoblast of woman destined to develop preeclampsia over produces atleast two antiangiogenic peptides that enter the maternal circulation- Soluble Fms- like tyrosine kinase 1 (sFlt-1), soluble endoglins (sEng).

Figure 4 – Balance between Pro angiogenesis and Anti Angiogenesis in PE - Normal
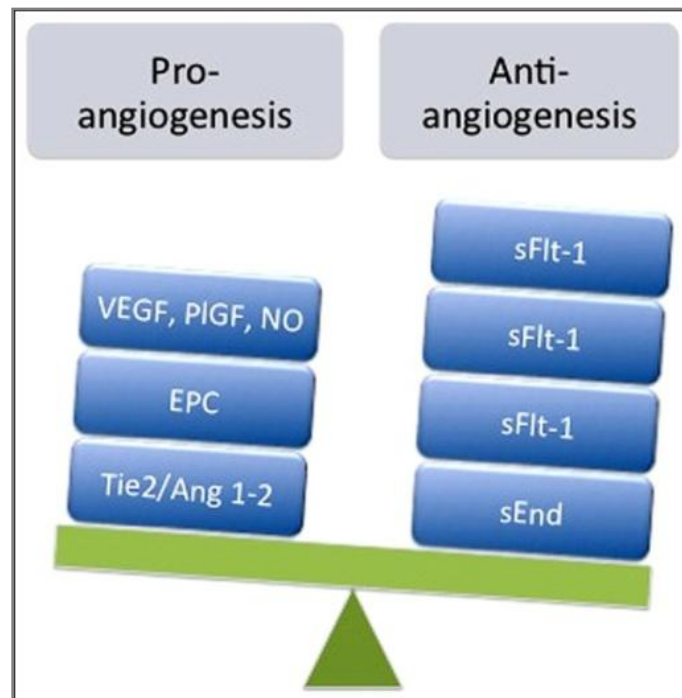
Vascular endothelial growth factors (VEGF) are endothelial specific growth factors plays a key role in promoting angiogenesis; placental growth factor (PLGF) is another member of VEGF family that is made predominantly in placenta. Activity of VEGF is mediated by interaction with two high affinity receptor tyrosine kinases: Kinase insert domain region (KDR) and fms like tyrosine kinase-1 (flt-1).These are expressed an endothelial surface. Alternative splicing of flt-1 results in production of sflt-1; this cannot attach to cell membranes and is secreted in to the maternal blood. It can antagonize VEGF and PLGF by binding to it and

preventing its interaction with endogenous receptors. Excess sflt-1 production is seen in pregnancy induced hypertension/PE placentas, which creates an antiangiogenic state and plays a causal role in the pathogenesis of maternal syndrome in pregnancy induced hypertension/PE. [49]

Figure 5 – Mechanism of sFlt-1 and sEng in causing PE.
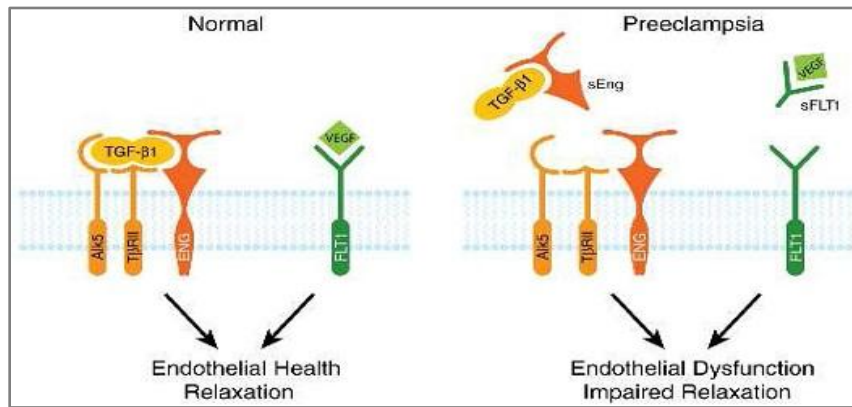
Soluble endoglin(sEng) is derived from placenta blocks endoglin, which is a surface coreceptor for the transformin growth factor β(TGFβ) family. sEng inhibits TGFβ from binding to endothelial receptors and results in decreased endothelial nitric oxide-dependent vasodilation.[48] VEGF is known to stimulate angiogenesis as well as to promote vasodilation by increasing production of nitric oxide and prostacyclin, signalling molecules that are decreased in pregnancy induced hypertension/PE. PLGF is important in vasculogenesis and control of microvascular permeability.[49]

PREDICITON OF PREECLAMPSIA

Measurement during early pregnancy – or across pregnancy – of various biological, biochemical, and biophysical markers implicated in the pathophysiology of preeclampsia has been proposed to predict the development. These testing strategies have poor sensitivity and poor positive predictive value for preeclampsia. Few tests are discussed below

1. **Roll over test (Gant's roll over test):** It measures the hypertensive response to woman at 28 to 32 weeks who are resting in the left lateral recumbent position and then roll over to supine position. Increase in blood pressure (diastolic BP by 20mm of Hg) signifies a positive test. In preeclampsia the positive predicitive value was only 33%, negative predictive value was 92%..Sensitivity is 20% and specificity is 93%.[57]

2. **Serum uric acid** – It is one of the early manifestation of PE. Plasma uric acid exceeding 5.9 mg/dl at 24 weeks had a positive predicitive value for preeclampsia by 33%. It likely results from reduced uric acid clearance from diminished glomerular filtration, increased tubular reabsorption and decreased secretion. Sensitivity – 0-55%,specificity 77-95%.[59]

3. **Fibronectin** : These high molecular weight glycoproteins are released from endothelial cells and extracellular matrix following endothelial injury. Increased plasma levels of fibronectin precedes the clinical signs of preeclampsia. The positive predicitive value was 29% but negative predictive value was 98%. Sensitivity is 50-83% and specificity is 43-94%.[61]

4. **Mean arterial pressure measurement:**

   - Elevated mean arterial pressure at least 85-90 mm of Hg in second trimester has been reported to have widely varying predictive ability.

   - The sensitivity of the screening test was 22.9% , specificity 92.5% , positive predictive value 25.0% and negative predictive value 91.7%.[56]

5. **Provacative pressor tests:**

   Three tests have been evaluated to assess the BP rise response to a stimulus.

6. **Isometric exercise test(Hand-Grip test):**

    The Hand-Grip test is positive when the systolic blood pressure increased 15 mmHg or more during isometric exercise or decreased 14 mmHg or more immediately after isometric exercise. The sensitivity, specificity, PPV and NPV are 81.8%, 68.4%, 20% and 07.5% respectively.[58]

7. **Serum biomarkers of fetal- placental unit endocrine dysfunction:**

    Several serum parameters have been proposed to predict PE. They include human chorionic gonodotropin(hcG), alpha-fetoprotein(AFP), estriol, pregnancy-associated protein A(PAPP A), inhibin A, activin A, placental protein 13(PP13), corticotropin-releasing hormone, A disintegrin, ADAM-12 and kisspeptin. Newer ones are continuously added. Many studies have been done to evaluate the value of them in prediction of PE but none are proven beneficial. The prediction value of the PAPP-A, AFP and uE3 is 0.032, with the specificity and sensitivity of 98.93% and 70.59%, respectively.

8. **Microalbuminuria:**

    Microalbuminuria is defined as excretion of albumin in urine at the rate of 30-300mg/day. Studies are showing that there is increased incidence of PE with presence of microalbuminuria at booking visit. As a predictive test for PE, microalbuminuria has sensitivity, specificity, PPV and NPV of 88.9%, 67.9%, 22.2% and 98.3% respectively.[60]

9. **Angiogenic and antiangiogenic factors**:

    The imbalance between proangiogenic and antiangiogenic factors is related to PE pathogenesis. Serum levels of proangiogenic factors like VEGF and PIGF decrease

before clinical manifestation of PE, at the same time levels of antiangiogenic factors like sFlt-1 and sEng increase.[62]

The sensitivity, specificity, PPV and NPV of **sEng** is 62.1%, 56.8%, 52.9% and 65.6% respectively. The sensitivity, specificity, PPV and NPV of **sFlt-1** is 44.8%, 67.6%, 52% and 61% respectively. The sensitivity, specificity, PPV and NPV of PIGF is 100%, 47.2%, 60.4% and 100% respectively. The sensitivity, specificity, PPV and NPV of **sFlt-1/PIGF** is 96.6%, 5.7%, 40% and 100%.[62] Their predictive accuracy is higher for early-onset PE.

10. Cell-Free Fetal DNA:

The novel technology of cell-free fetal DNA (cffDNA) testing in maternal serum is commonly used for prenatal aneuploidy screening but may demonstrate other predictive applications. Higher levels of cffDNA have been found in women who develop PE and are thought to be secondary to accelerated placental apoptosis from hypoxia and oxidative stress in placental insufficiency.[63] Significantly elevated levels are seen in early-onset or severe PE and precede any clinical symptoms.

Maternal ethnicity, BMI, and smoking status are known to affect cffDNA levels, but these confounding factors have not been adequately controlled for in earlier studies. Rolnik et al. demonstrated an increase in median total cff DNA and a decrease in median fetal fraction at 11–13 weeks in women who subsequently developed early-onset PE.[64] However, the results were not statistically significant once converted to multiples of median and adjusted for maternal characteristics, and the authors concluded that cffDNA levels are not predictive of PE in isolation.

11. Proteomic, metabolomic and transcriptomic markers:

Study of serum and urinary proteins and cellular metabolites are the newer advances in the prediction of PE. Preliminary studies indicate that they may be useful.

12. Oxidative stress: Increased level of lipid peroxide coupled with decreased activity of antioxidants is seen in woman with preeclampsia. Malondialdehyde is a marker of lipid peroxidation. Other markers are hyperhomocystinemia causes 3 to 4 fold risk of PE.

13. Cytokines

Elevated levels of various cytokines like some interleukins, Tumour Necrosis Factor – alpha and C-reactive protein are noted in woman with PE

14. Biochemical markers: Due to inflammatory cascade, number of placental peptides are released like corticotrophin-releasing hormone, chorionic gonadotrophin, pentraxin 3 (PTX-3), P-Selectin, pregnancy associated plasma protein A (PAPP-A) activin A and inhibin A. Elevated levels of antiangiogenic factors are associated with PE.

15. UTERINE ARTERY DOPPLER VELOCIMETRY

Doppler ultrasound of the uterine artery impedance in the first trimester has been used as an early screening for preeclampsia. Alteration in the uterine artery PI predicts the onset of the disease.

Normally uterine artery PI decreases with gestation. The decrease in the impedance to flow with gestation is presumably the consequence of physiological trophoblastic invasion of maternal spiral arteries.

Many studies evaluated the worth of the abnormal uterine artery doppler studies in prediction of PE both in first and second trimesters. In first trimester the sensitivity of 24% and PPV of 11% is reported by Gomez et al.[65] In second trimester sensitivity of 76.9%, a specificity of 52.9%, a PPV of 10.2%, and a NPV of 97.1%, respectively are reported in prediction of PE.[66]

ANATOMY OF UTERINE ARTERIES

Uterus receives its blood supply from uterine and ovarian artery.

Figure 6 – Anatomy of Uterine artery.
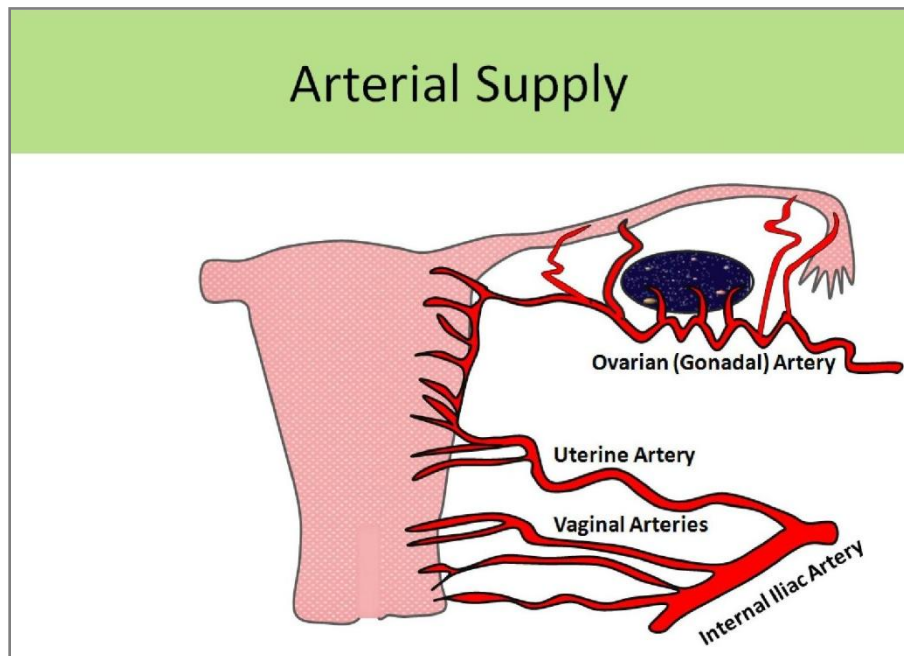
Uterine artery arise from the anterior trunk of the internal iliac (or hypogastric artery). It reaches the uterus at the level of internal os ,slides upwards spirally along the lateral border of uterus to the region of uterine cornua and finally anastomose with the ovarian artery.

Uterine artery –> Arcuate –> Radial –> Basal –> Spiral and straight arterioles of the functional layer of endometrium.

Figure 7 – Anatomy of Uterine Artery(b)
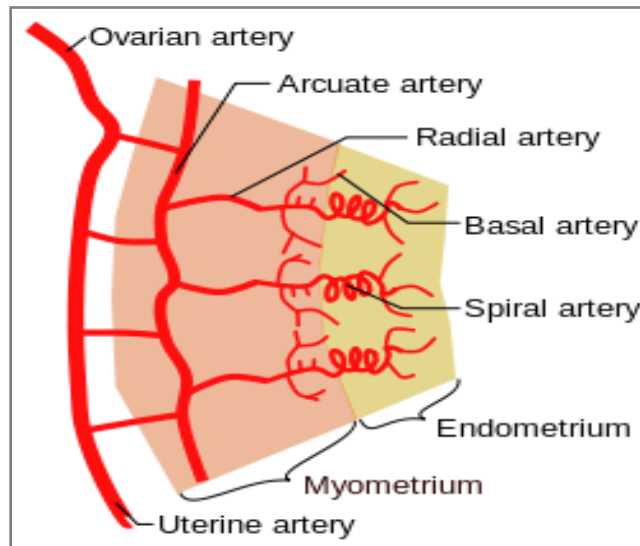
Ovarian arteries arise from the aorta, just below the level of the level of renal arteries.

PHYSIOLOGY OF UTEROPLACENTAL CIRCULATION

Placenta is a unique vascular organ that receives blood supply from both maternal and fetal systems.

1. The maternal – placental (uteroplacental) circulation

   Here circulation starts with the maternal blood flow into the intervillous space through decidual spiral arteries. The inflow maternal arterial blood pushes deoxygenated blood into the endometrial and then uterine veins back to the maternal circulation.

2. The fetal - placental (fetoplacental) blood circulation

   This allows the umbilical arteries to carry deoxygenated blood and nutrient depleted fetal blood from the fetus to the villous core to the vessels. The umbilical vein carries fresh oxygenated and nutrient rich blood circulating back to the fetal circulation. At term, maternal blood flow to the placenta is approximately 600-700ml per minute. The functional maternal-fetal exchange takes place at terminal villi.

DOPPLER ULTRASOUND:

Doppler ultrasound provides a non-invasive method for the study of fetal hemodyanamics. Investigation of the uterine and umbilical arteries gives information on the perfusion of the uteroplacental and fetoplacental circulation, respectively, while Doppler studies of selected fetal organs are valuable in detecting the hemodyanamic rearrangements that occur in response to fetal hypoxemia.

Direct measurement of the uterine artery blood flow was obtained by means of electromagnetic technique.

PRINCIPLE OF DOPPLER:

The Doppler effect is defined as the observed changes in the frequency of transmitted waves when relative motion exists between the source of the wave and the observer. The frequency increases when the source and the observer move closer and decreases when they move apart.

Figure 8– Doppler Effect(a)
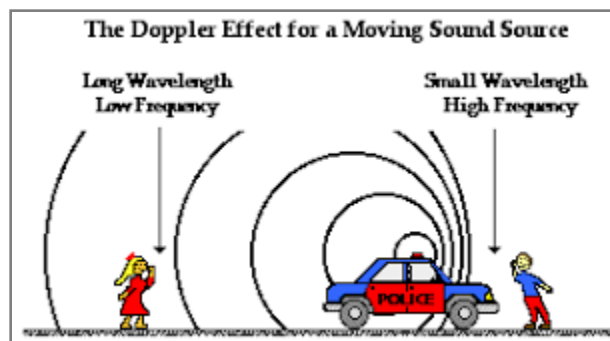
This phenomenon bears the name of the discoverer, Christian Andrews Doppler, an Austrian mathematician and physicist in 1842. The change in frequency of the energy wave transmission is known as the Doppler frequency shift or simply the Doppler shift.

Figure 9 – Doppler Effect
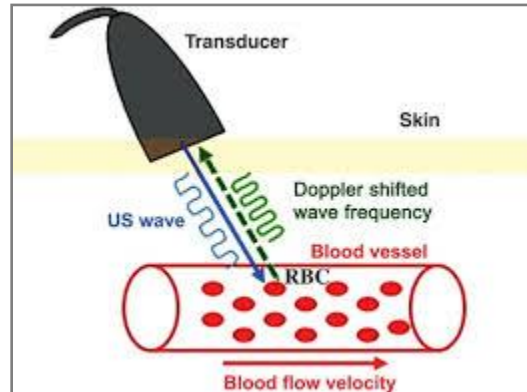
fd = ft – fr *: fd* – is the Doppler shift frequency

ft is the transmitted frequency

fr is the received frequency.

The change in frequency of the energy wave transmission is known as the Doppler frequency shift or simply the Doppler shift.

The Doppler effect is observed irrespective of whether the observer or the source moves.

DOPPLER VELOCIMETRY:

Qualitative assessment: Achieved usually by analysing the waveforms or the colour distribution. Blood flow can also be qualitatively assessed by listening to Doppler signals.

Quantitative assessment: Allows assessment of velocity. Doppler measurement can be considered reliable as long as the insonent angle is 60 degrees. Velocity measurements most commonly in pulsed Doppler are maximum peak systolic velocity, highest time averaged maximum velocity and minimum diastolic velocity.

Semi-quantitative assessment: The relationship between systolic and diastolic components of waveforms is evaluated and angle dependence which is important in quantitative measurements becomes less important. Commonly used indices available on most commercial scanners are

1) Resistance index (RI) (Also called resistive index or Pourcelot's index)

   RI = (peak systolic velocity – end diastolic velocity)/peak systolic velocity [(S-D)/S]

2) Systolic /Diastolic ratio (S/D, sometimes called A/B ratio)

3) Pulsatility index (P/I) =(S-D)/A

   PI = (peak systolic velocity – end diastolic velocity)/ time averaged velocity.

Figure 10 – Doppler Indices

S = systolic peak (max. velocity)
D = end diastolic flow
Vm = mean velocity
A = Temporal average frequency over 1 cardiac cycle

Doppler Indices
RI = (S - D) / S (Pourcelot, 1974)
PI = (S - D) / A (Gosling, 1976)
S/D Ratio = S/D (Stuart & Drumm, 1980)
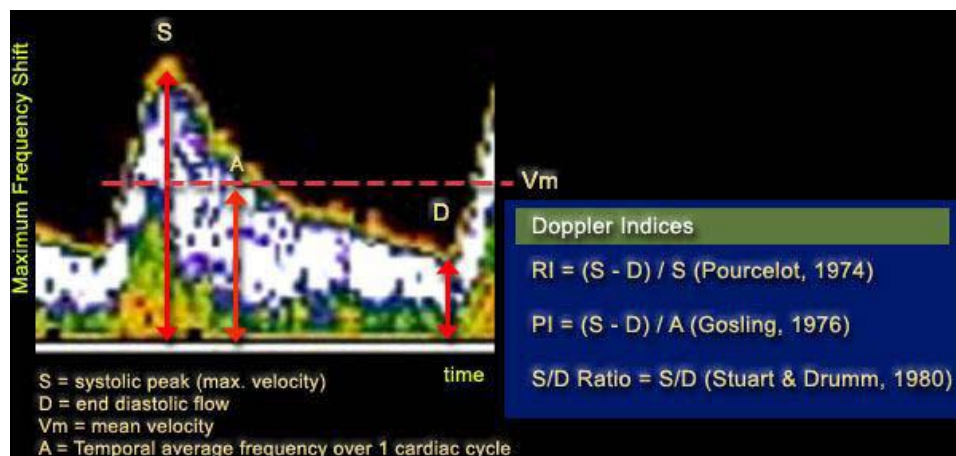
These indices are all based on the maximum Doppler shift waveform. The PI takes slightly longer to calculate than the RI or S/D ratio because of the need to measure the mean height of the waveform PI is a better index in obstetric Doppler because,

- When diastolic velocity =0, RI will always be 1, whereas PI could be any value more than 1. So PI is more informative in such situations

- PI takes the entire waveform into account and not just the maximum and minimum frequencies as in RI.

Doppler study of Uteroplacental circulation

Using Doppler as a screening test, several studies have demonstrated an association of abnormalities in the flow velocity waveform of uterine arteries with the subsequent development of PE, fetal growth restriction(FGR), placental abruption and preterm delivery.

The morphologic changes in the uterine vasculature can be demonstrated by the color and pulsed Doppler with detection and analysis of main uterine arteries and their ramifications into arcuate and radial arteries upto their spiral artery terminal branches. The blood flow velocity increases in the uteroplacental circulation, while its impedance decreases as gestation advances.

The criteria adopted from studies on uteroplacental circulation for obtaining the flow velocity waveform have been distinct. There are reports on evaluation of the arcuate and the radial arteries,[69] in the uterine artery and arcuate artery on the placental and the contralateral sides, besides utilization of average values of right and left uterine arteries. The study of the subplacental arteries or the arcuate arteries in just one of the sides of the uterus is not representative of the whole uterine flow. The alterations in the placental arcuate arteries appear only in more advanced phases of the pathologic processes, and do not allow an early diagnosis.[70]

Uterine artery Doppler in normal pregnancy :

In non pregnant state there is rapid rise and fall in uterine artery flow velocity during systole and a "notch" in the descending waveform in early diastole.[71] During pregnancy, they noted a significant increase in uterine artery compliance between 8 and 16 weeks, which continued to a lesser extent until 26 weeks gestation.[72] These changes are reflected in RI and PI of uterine artery Doppler signal.

Figure 11 - Uterine artery Doppler wave forms
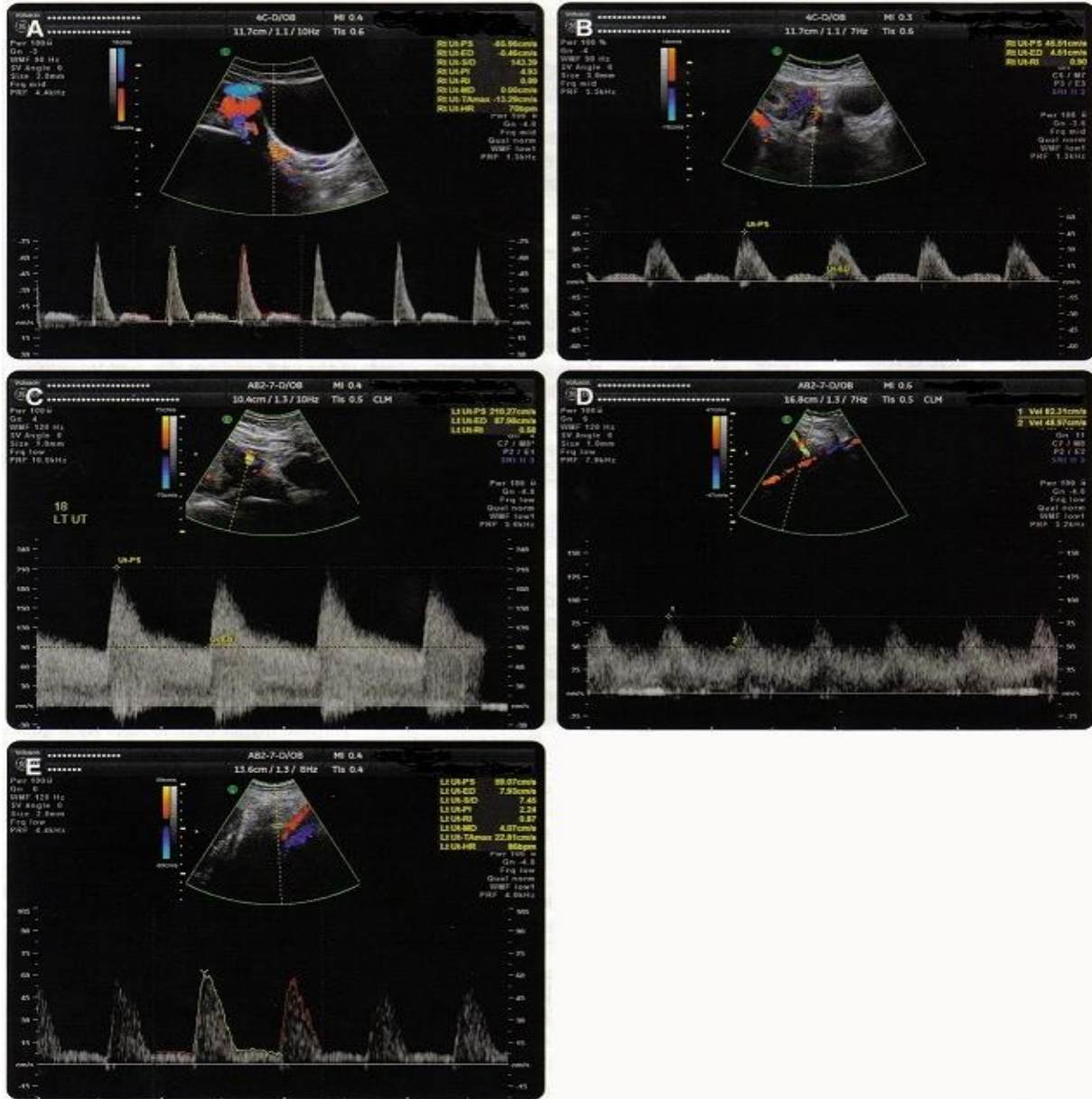
A- Nonpregnant patient.   B- First trimester.

C - Second trimester ,   D- Third trimester

E- Abnormal uterine artery Doppler wave form demonstrating high resistance

Persistence of high impedance to blood flow is observed in the uterine arteries of women with PE, which is another indirect evidence of abnormal placentation.[73] It is therefore logical that many studies has focused on uterine artery Doppler as a screening test of women at risk of developing PE.

e. Criteria for abnormal test:

Uterine artery Doppler is considered abnormal when

PI is > 95th centile (>2.3 in our study- [Both average and single]).

DOPPLER STUDY OF UTEROPLACENTAL CIRCULATION:

Using Doppler as a screening test, several studies have demonstrated an association of abnormalities in the flow velocity waveform of uterine arteries with subsequent development of preeclampsia, IUGR, Placental abruption and preterm delivery. The morphologic changes in the uterine vasculature can be demonstrated by the colour, and pulsed Doppler with deduction and analysis of main uterine arteries and their ramifications into arcuate and radial arteries upto their spiral artery terminal branches. The blood flow velocity increases in the uteroplacental circulation, while its impedance decreases as gestation advances.

The placenta due to its implantation and development, modifies the uterine circulation from low flow with high resistance to high flow with low resistance. The abnormal Doppler study of the uterine arteries in the early first trimester signifies defective placentation, which is detected by the average PI (>2.3).

Using Doppler ultrasound, the main branch of uterine is easily located at the cervico corporeal junction with the help of real time color imaging. Doppler velocimetry measurements are usually performed near to its location, either transabdominally or transvaginally,

TRANSABDOMINAL TECHNIQUE :

- Transabdominally, the probe is placed longitudinally in the lower lateral quadrant of the abdomen, angled medially. Colourflow mapping is useful to identify the uterine artery as it is seen crossing the external iliac artery.

- The sample volume is placed 1 cm downstream from the cross over point.

- In a small proportion of cases if the uterine artery branches before the intersection of the external iliac artery, the sample volume should be placed on the artery just before the uterine artery bifurcation.

- The same process is repeated for the contralateral uterine artery

- With advancing gestational age, the uterus usually undergoes dextro-rotation. Thus, the left uterine artery does not run as lateral as the right.

TIMING OF SCREENING

Screening of PE by uterine artery Doppler assessments is possible from at least 11 weeks of gestation. Trophoblastic invasion is maximal in the 1st trimester and PE develops from a relative failure of this event, validates the evaluation of uterine artery Doppler assessment in the 1st trimester.[77] However screening too early leads to false positive rates and lower PPVs as what appears to be abnormal uterine artery Doppler waveforms in early second trimester may fully develop and normalize by late second trimester.

TRANSVAGINAL TECHNIQUE

- Transvaginally, the probe is placed in the anterior fornix. Similar to the transabdominal technique, the probe is moved laterally to visualise the paracervical vascular plexus and the above steps are carried out in the same sequence as for the transabominal technique.

- The measurement should be repeated independently for the right and the left utrine arteries, The average of both is taken and the risk is assessed.

REVIEW OF LITERATURE

- In 1995, van den Elzen et al,[83] reported on 352 women aged 35 years and older. Using Doptek, the PI was measured at 12 to 13 weeks of gestation, and this was associated with the development of hypertensive disorders and FGR. When the PI was in the upper quartile the risk of PE was increased by a factor of four when compared to women in which PI was in the lower quartile.

- Martin et al,[80] conducted the the largest screening multicenter study to date. Transabdominal examination of the uterine arteries was carried out at 11 to 14 weeks in unselected population. The sensitivity of mean uterine artery PI above 95th percentile (2.35) was 27.0% for PE. The study showed that early diastolic notches were present in 55% of cases, limiting their use for screening at this gestation. The sensitivity for complications requiring delivery before 32 weeks was 60%.

- In the study conducted by Gomez et al,[65] where 999 pregnant women were examined between 11 to 14 weeks during routine scan using transvaginal color and pulsed Doppler. The authors found a significant change in the 95th percentile of mean uterine artery PI with advancing gestation. They reported a progressive decrease in the prevalence of bilateral notching and PI with gestation. There were 22 cases of PE, and using a cut-off of PI above the 95th percentile, the sensitivity, specificity, PPV and NPV were 245, 95.1%, 11.3% and 97.9% respectively. The authors of the study acknowledged the potential advantages of early screening for PE and associated complications, but concluded that there is a limited role for uterine Doppler velocimetry in identifying the pregnancies with increased risk of developing hypertensive disorders.

- In the prospective study conducted by Pilalis et al,[84] 878 women were undergone routine prenatal ultrasound examination at 11 to 14 weeks, pulsed wave Doppler was used to obtain uterine artery flow velocity waveforms and mean PI of the uterine arteries was calculated and maternal serum samples for PAPP-A were assayed. The sensitivity of mean uterine artery PI > 95th percentile in predicting PE and abruption were 23.1% and 42.8%% respectively. The authors noted that independent predictors of subsequent development of PE were mean uterine artery PI > 95th percentile and maternal history of PE/ hypertension. Increased uterine artery PI was the only independent factor in the prediction of placental abruption. The combination of uterine artery PI and maternal history of PE/ hypertension was better predictor tha using uterine Doppler alone in predicting PE.

- Plasencia et al,[85] investigated the performance of screening for PE using maternal characteristics such as body mass index, age, ethnic origin, smoking, medical and obstetric history and uterine artery PI in the first trimester. They concluded that in unaffected individuals log MoM PI was influenced by maternal ethnic origin, body mass index, previous history of PE and fetal crown-rump length. In the prediction of PE significant contributions were provided by log MoM PI, ethnic origin, body mass index and previous and family history of PE. They also added that for a false-positive rate of 10% the predicted detection rate of PE requiring delivery before 34 weeks was 82%, compared to 31% for late PE, 12% for gestational hypertension and 18% for small for gestational age.

- Harrington et al,[86] conducted a follow up study in 652 women with singleton pregnancies who had transvaginal uterine artery and umbilical Doppler examination

performed at 12-16 weeks of gestation. Measurements include presence/absence of an early diastolic notch, vessel diameter, RI, PI, time averaged mean velocity, maximum systolic velocity and volume flow in the right and left uterine arteries and RI and PI in umbilical arteries. They concluded indicative of a failure to modify the uterine artery circulation in early pregnancy are associated with premature delivery(odds ratio 2.38), development of PE(odds ratio 42.82)and SGA baby(odds ratio 8.61).

- Melchiorre et al, conducted a study in 3058 singleton pregnant women at 11-14 weeks of gestation. They measured mean RI and presence of early diastolic notch was recorded. They concluded that sensitivity and specificity of RI > 95th centile was 24.2% and 95.8% respectively in predicting preterm-PE. Early diastolic notch was present in 44.7% of normal pregnancies so cannot be used for screening. There were no significant differences in first-trimester mean uterine artery RI (P = 0.136) or prevalence of bilateral notches (P = 0.459) between women who had a normal pregnancy outcome and those who developed pre-eclampsia at term. These data demonstrate that increased uterine artery RI in the first trimester is associated with the development of preterm, rather than term, pre-eclampsia and provide supportive evidence for the hypothesis that these disorders may have different etiologies.[77]

PREVENTION OF PREECLAMPSIA

Prevention of PE, if possible, would be a great in antenatal care.

Primary prevention: Avoiding the occurrence of the disease by avoiding the risk factors.

Secondary Prevention: Allows breaking off the disease process before the emergence of **obvious clinical disease i.e, Early diagnosis and treatment.**

Tertiary Prevention: Prevention of complications caused by the disease process i.e treatment.

PRIMARY PREVENTION:

Primary Prevention may be possible to some extent by the modification of some of the risk factors of PE. As the disease occurs more often in nulliparous women or in multiparous women with change of partners, there appears to be a protective effect of long term sperm exposure on the frequency of the disease. Hence, it is recommended to have pregnancies with low-risk men, to stay with the same partner and to have children at an age when the endothelium is still able to cope with the inflammatory stress associated with pregnant state. Prevention or effective treatment of obesity could result in a significant reduction in the frequency of PE and should be encouraged. Similarly, women with Diabetes, Chronic Hypertension, renal and other medical disorders should have their primary condition under control before venturing into conception.[88]

SECONDARY PREVENTION:

Secondary prevention of any disease is feasible if the following 3 basic requirements are fulfilled and are available.

1. Accurate knowledge of the patho-physiological mechanisms

2. Availability of effective screening methods

3. Means of intervention and modification of patho-physiology

Unfortunately, in-spite of extensive research world-wide, none of the three criteria are available for pre-eclampsia to make a strong case for successful secondary prevention. The

multi-factorial origin of the disease suggests that it is highly unlikely that there will be a single predictive test available in future to predict PE.

A. Non-Pharmacological Interventions

B. Nutritional Interventions

C. Pharmacological Interventions

A. Non-Pharmacological Interventions

Bed Rest : It is recommended initially for women at high risk of developing PE in the hope that it reduces oedema and lowers blood pressure by increasing urinary output. However, bed rest was not found to be effective to prevent PE , modify the disease, decrease the incidence of pre-term delivery, low birth weight or the perinatal mortality. In fact, bed rest can be harmful to pregnant women and should not be routinely recommended.

Life- Style Changes: Regular ante-natal care is mandatory for the prevention and early detection of PE. Job stress including lack of control over work place, timing and frequency of breaks may be related to various adverse events including PE. But no studies confirms the association, more research is required in this field.

Regular Physical Activity: Regular pre-natal exercise may prevent or oppose the progression of the disease as suggested by epidemiological studies. The protective effect results from one or more of the following mechanisms:[89]

• Stimulation of placental growth and vascularity

• Reduction of oxidative stress

• Exercise induces reversal of maternal endothelial dysfunction.

B. NUTRITIONAL INTERVENTIONS:

Dietary Sodium Restriction: Although sodium and water retention are universal in pregnancy, there are no differences in total body water or serum sodium concentration between women with mild or severe PE as compared to gestationally age matched pregnant women without hypertension. Dietary sodium restriction has been found to be useful in long-term management of chronic hypertension in men. However, there is no convincing evidence of its efficacy in prevention or treatment of hypertension during pregnancy.[90]

Dietary Protein and Energy Intake : Several nutritional interventions have been suggested to prevent PE including increasing protein and energy intake or restricting protein or energy intake for obese women. However, a recent overview of randomized trials of nutritional interventions during pregnancy reported no benefit of such measures in the prevention of PE.[91]

Control of Obesity: Although obesity is a known risk factor for superimposed PE, there is no evidence that limiting weight gain during pregnancy reduces its occurrence.

Fish Oils : Inclusion of fish oils in the diet, Eicosapentenoic acid and docosahexanoic acid, was shown by some studies to have a protective effect in the preventin of PE. They inhibit the synthesis of arachidonic acid.[92]

In addition, Eicosapentenoic acid competes with arachidonic acid as the the substrate for cyclo-oxygenase, inhibiting the production of thromboxane A2 by the platelets and producing low amounts of physiologically inactive thromboxane-A3. However several multicentric trials failed to reduce the risk of PE or FGR.

Alcohol Intake: There is no definite evidence that consumption of less than 120 ml of alcohol per week causes any adverse effects on pregnancy outcome including fetal growth. Not evidence to suggest alcohol at excess quantities can cause PE.

Arginine Supplementation: Few studies have documented that dietary supplementation with L-Arginine has been found to be useful in the prevention of PE. But as such there is no strong evidence to suggest L-Arginine supplementation prevents PE.

C. PHARMACOLOGICAL INTERVENTIONS:

Role of Antihypertensive drugs: It is known that women with pre-existing chronic hypertension are at significantly higher risk of developing PE than their normotensive counterparts. The various anti-hypertensive medications like Methyldopa, Labetalol and Atenolol have been evaluated in various randomized trials for their efficacy in prevention of superimposed PE.[93] Critical analysis of all these trials failed to find any reduction in the incidence of PE.

Role of Diuretics: A meta-analysis of 9 randomised trials using diuretics in pregnancy revealed no reduction in the incidence of PE or perinatal mortality, although the incidence of oedema and hypertension was reduced.[94] Due to the deleterious effects such as reduced renal and placental perfusion, diuretics should not be recommended in PE.

Zinc Supplementation: Zinc concentration is reduced among women with hypertensive disorders of pregnancy.[95] Recent randomized clinical trials have failed to demonstrate the efficacy of zinc supplementation for the prevention of PE.

Magnesium supplementation: Magnesium has a proven benefit for the prevention and treatment of severe PE and eclampsia. Hence it was implicated that deficiency of magnesium

was important in the pathogenesis of PE.[96] A Cochrane review of two trials could detect no apparent effect of magnesium supplementation on the prevention of PE.

Role of low dose aspirin: The abnormalities of vasospasm, endothelial cell dysfunction and activation of coagulation- haemostasis systems are probably caused by an imbalance in the production of prostaglandins, PGI2 (vasodilator and inhibitor of platelet aggregation) and TXA2 (Vasoconstrictor and platelet aggregator), with the balance tilted in favour of TXA2. Low dose aspirin (50-150mg /day) therapy during pregnancy selectively inhibits platelet TXA2 biosynthesis with minimal effects on PGI2 production.[97]

Multiple clinical trials including the **CLASP** study concluded that the overall use of low dose aspirin in pregnant women was associated with a 12% reduction in the incidence of PE and 19% reduction in the pre-term delivery in the high risk group. Thus the only group in whom Low dose Aspirin may be justified are those specially at high risk for early onset PE.

Role of Folic Acid and other B-Vitamins: Women with PE have been shown to have elevated levels of homocysteine which occur prior to the onset of the disease. Elevated levels of homocysteine may damage the lining of blood vessels leading to signs and symptoms of PE. Homocysteine concentrations have also been weakly and negatively correlated with the plasma folate concentration.[98] Few trials have so far shown a reduction in the incidence of PE following Vitamin B6 and folic acid. Although the metabolic correction of hyper homocysteinemia occurs, it is unknown currently whether or not metabolic correction translates into improved perinatal and maternal outcome.

Role of Heparin: Subcutaneous heparin alone or more often in combination with low dose aspirin has been used to prevent PE with significant reduction in its incidence. The scientific

basis for using heparin is to modify the endothelial cell dysfunction and the activation of the coagulation system, which are central in the pathophysiology of PE. There is, however, insufficient data available to recommend its use routinely in the prevention of PE except in Anti-phospholipid Syndrome.[99] Moreover, its use can cause adverse reactions like increased chances of spontaneous abortion, abruptio placentae, post partum haemorrhage and osteoporosis in the mother.

Calcium Supplementation: Data from epidemiological and observational studies have shown that there is an inverse relationship between calcium intake of 2 gms/day and the frequency of PE and eclampsia. This effect was greatest in women at high risk of hypertension and those with low baseline calcium intake.[100]

Role of Nitric Oxide Donors: Nitric oxide is a major paracrine mediator released by the endothelial cells. It is a potent vasodilator and inhibits platelet aggregation and adhesion to the vascular endothelial surfaces. Research indicated that PE is characterized by impaired NO (nitric oxide) synthesis with diminished production of second messenger cyclic guanosine monophosphate (cGMP). Small studies have shown the beneficial effects of Nitric oxide donors like transdermal glyceryl trinitrate patch 5mg/day in improving placental flow and uteroplacental perfusion in women with PE. Large multicentric trials are under way in various hospitals.[101]

Role of Antioxidants: Oxidative stress seems to play a major role in the aetiopathogenesis of PE. Oxidative stress markers are significantly raised while anti-oxidants are concomitantly reduced in maternal tissues, deciduas and placenta. Many trials have been completed with promising results. Chappell et.al [102] identified high risk women by history and by abnormal

uterine artery Doppler at 20 weeks. They randomized women at 20 weeks to receive either 1000 mg of Vitamin C and 400 IU of Vitamin E. There was a significant reduction in the markers of endothelial Activation. Plasminogen Activator Inhibitor ratio (PAI-1/PAI-2 ratio) . There have been many studies on the role of various antioxidants like vitamin C & E, lycopene, selenium, N-Acetyl cysteine and garlic in the prevention of PE. The use of antioxidant lycopene 2 mg twice daily from 16-20 weeks of gestation and continued treatment until delivery was found to have a significant reduction in PE. The incidence of FGR was also significantly lower. Results of larger trials are yet to be published.

OBSERVATION AND RESULTS

This is a prospective observational study conducted in 150 women at the Department of Obstetrics and Gynaecology, PSG Institute of Medical Sciences and Research centre, Coimbatore, Tamil Nadu. Based on the uterine Doppler value, my study population (n – 150) is divided equally (each 75) into control and case group. In the case group uterine artery Doppler value, both single uterine artery Doppler and average uterine Doppler $\geq$ 2.3 is considered as abnormal. Both the control and case group were followed up throughout the gestation for the development of adverse pregnancy outcome such as PE, gestational hypertension, eclampsia, IUGR and oligohydramnios.

Table –5 Age wise distribution of the study

AGE	CONTROL	CASES	TOTAL	(%)
< 20	9	5	14	9%
21 - 25	32	32	64	43%
26 – 30	29	27	56	37%
31 – 35	5	9	14	9%
> 35	0	2	2	1%
Total	75	75		

Figure –12 Age wise distribution of study population

Age Distribution [N=150][p>0.05]

	< 20	21 - 25	26 - 30	31 - 35	> 35
CONTROL	12%	43%	39%	7%	0%
CASES	7%	43%	36%	12%	3%
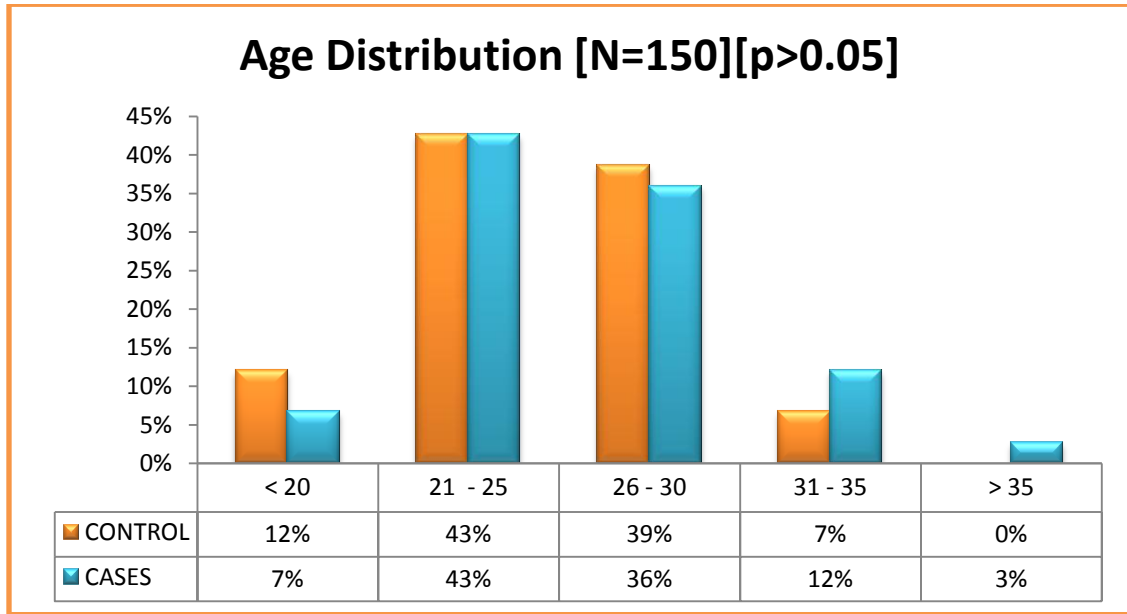
Table −5 and figure 12 show that out of 150 patients studied, 43% were between 21 − 25 yrs of age in both the groups,39% & 36% were between 26 and 30.There is no significant differences between the groups(p>0.05)

Table –6 Shows the mean age distribution in study group

Age	Mean	SD	Std. Error	95% CI for Mean		Minimum	Maximum	Sig
				Lower	Upper			
Mean Age with study Groups								
CONTROL	25.2	3.484	0.402	24.4	26	19	34	
CASES	26.13	3.905	0.451	25.23	27.03	18	39	>0.05

The distribution of ante natal mean age of both the groups had 25.2+/-3.48 & 26.13+/-3.91.There is no significant difference between the groups(p>0.05)

Of the age group distribution the youngest one is 18 years and the eldest women is 39 years.

Table – 7 Parity status of the study population

Parity	Control	Cases	Total	(%)
PRIMI	38	43	81	54%
MULTI	37	32	69	46%
Total	75	75		

Figure -13 Parity status of study population

PARITY [N=150][p>0.05]	PRIMI	MULTI
CONTROL	51%	49%
CASES	57%	43%
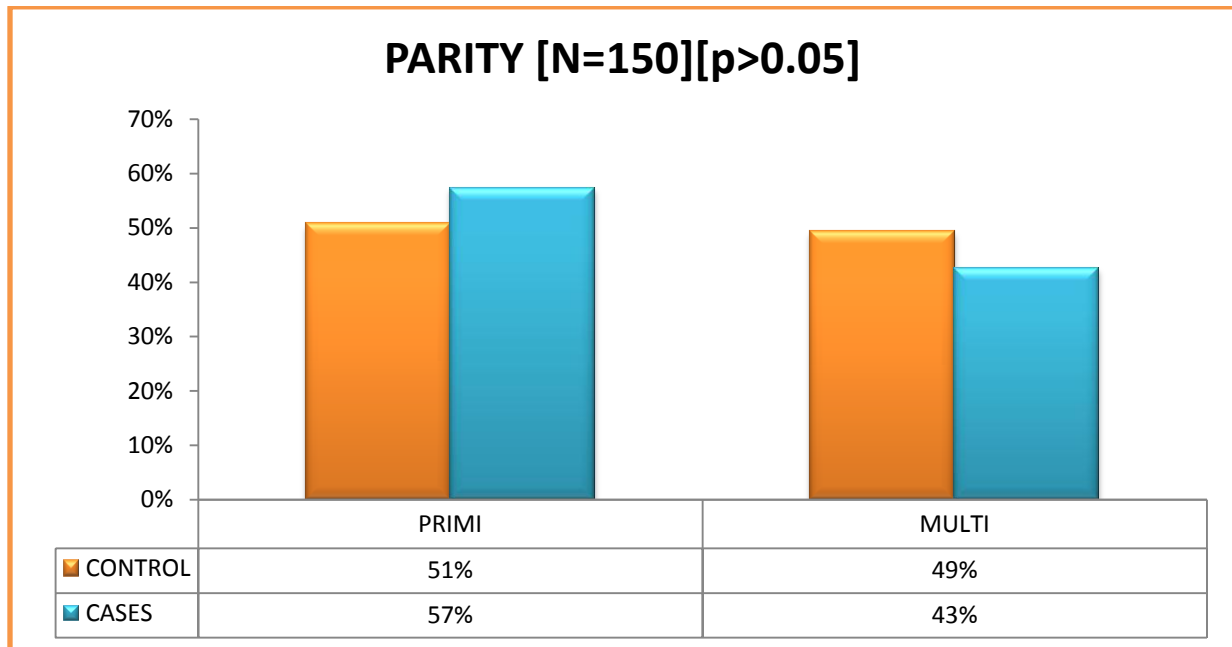
Table – 7 and Figure – 13 shows the parity status of the 150 women in the study. Maximum women i.e 54% are primigravida . Youngest primi being 18 years and eldest primi is 35 years old. 46% are multi, youngest multi is 21 years and eldest multi is 39 years old.

Table –8 Family history of study population

Family History	Control	(%)	Cases	(%)
YES	5	7%	14	19%
NO	70	93%	61	81%
Total	75		75	

Figure –14 Family history of study population
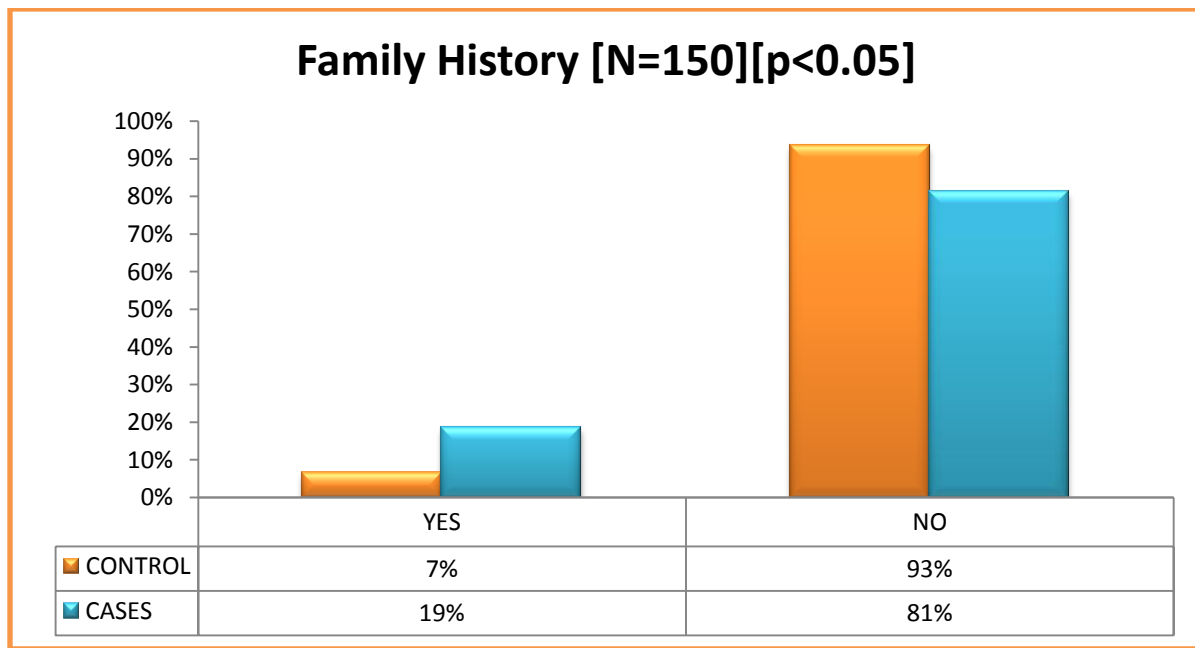
Table –8 and Figure –14 shows the family history of study population. About 7% and 19% of women in control and cases group have significant family history. Family history of Diabetes Mellitus(DM), Hypertension(HTN), DM and HTN included in this. There is no significant family history of preeclampsia or eclampsia found in these groups.Family history is insignificant in my study group for adverse pregnancy outcome.

Table –9   Medical history of the population in the study

Other medical History in the Population of the Study Groups			
Medical Disorders	**Case**	**Control**	**Total**
Over Hypo Thyroid	3	2	5
Type II DM	1	0	1
GDM on Diet	4	6	10
GDM on Drugs	5	2	7
Chronic Hypertension	1	0	1
Total	14	10	24
(%)	19%	13%	16%
Unaffected	61	65	126
(%)	81%	87%	84%

Figure – 15 Medical history of the population in the study

Other Medical History in the Study Population [N=75][p<0.05]

	Medical Disorders	Unaffected
CASE	19%	81%
CONTROL	13%	87%
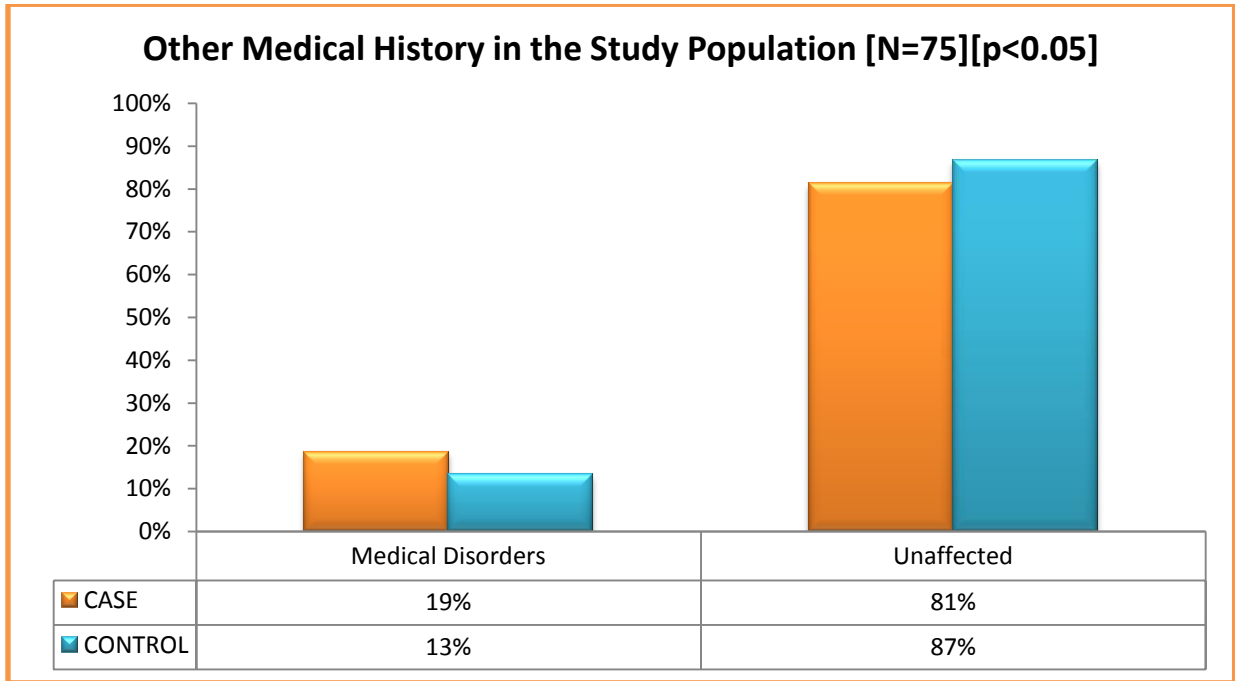
Table –9 and Figure – 15 shows the medical history of the study population. History of other medical disorders such as overt hypothyroid, Type 2 DM, GDM on diet/OHA,Chronic hypertension are included. In case group ,1 patient with history of chronic hypertension present. There is no significant difference in the case and control group with the medical history.

Table -10 Previous obstetric history of the study population

Significant	Study Group			
History	Control	(%)	Case	(%)
BOH	1	1%	4	5%
PE	0	0%	1	1%
NIL	74	99%	70	93%
Total	75		75	

Figure –16 Previous obstetric history in the study population
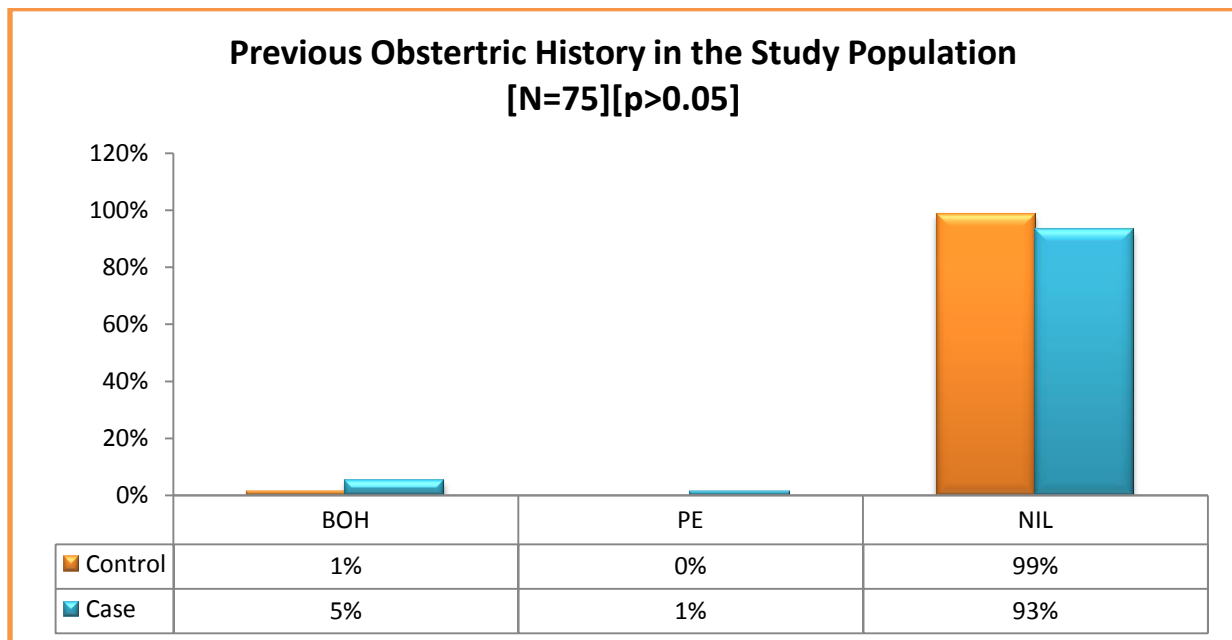
Table –10 and Figure –16 shows previous obstetric history in the study population. In the study group 3% history of BOH present. In the case group 5% has BOH due to 2 Neonatal death and 2 term IUD.

Table – 11 Shows Uterine artery Doppler value ranges in both case and control group

Uterine Artery Doppler	Control	(%)	Cases	(%)
< 1.49 (<50th Percentile)	44	59%	0	0%
1.5 - 2.29 (>50th - 95th Percentile)	31	41%	0	0%
≥ 2.3 (≥95th Percentile)	0	0%	75	100%
Total	75		75	

Figure – 17 Shows Uterine artery Doppler value ranges in both control and case group

Uterine Artery Doppler Value [N=150]	< 1.49 (<50th Percentile)	1.5 - 2.29 (>50th - 95th Percentile)	> 2.3 (95th Percentile)
CONTROL	59%	41%	0%
CASES	0%	0%	100%
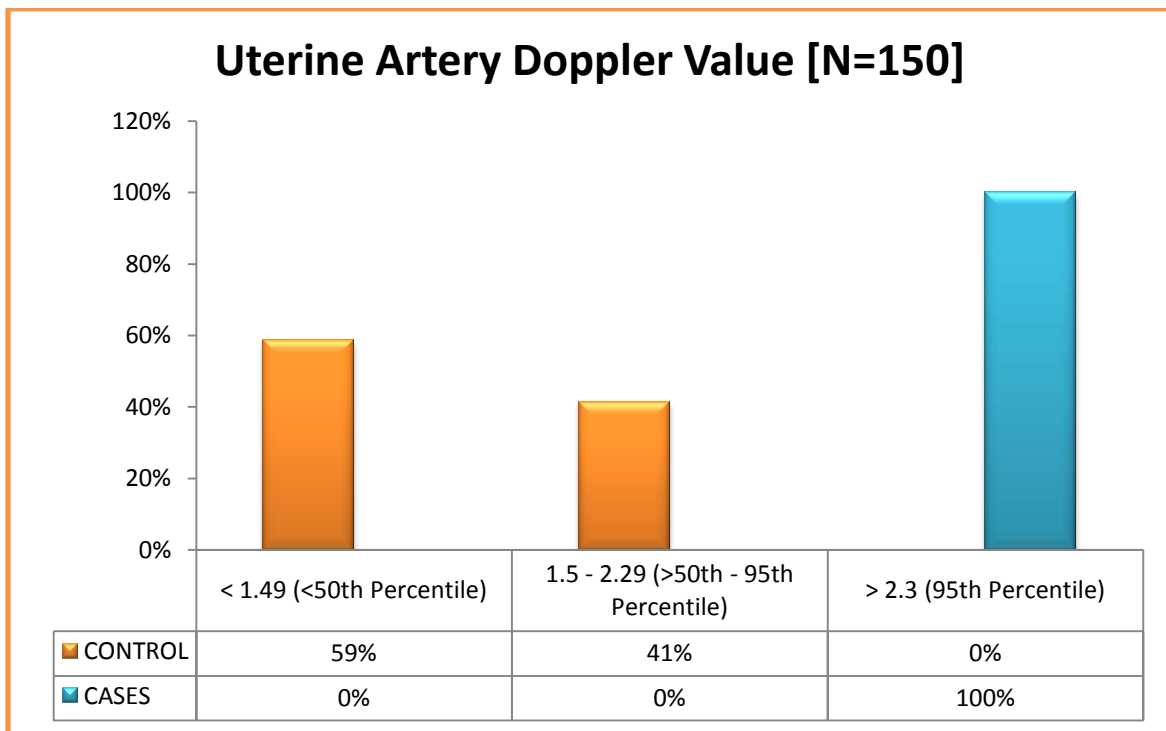
Table –12 Shows the mean of clinical variables in the study group

		Mean	SD	Std. Error	95% CI for Mean Lower Bound	95% CI for Mean Upper Bound	Minimum	Maximum	Sig
U/A L	Control	1.40	0.41	0.05	1.31	1.50	0.58	2.28	
	Cases	2.3	0.65	0.08	2.11	2.41	0.5	4	<0.001
	Total	1.83	0.69	0.06	1.72	1.94	0.5	4	
U/AR	Control	1.45	0.42	0.05	1.36	1.55	0.48	2.26	
	Cases	2.3	0.71	0.08	2.13	2.46	0.78	4.6	<0.001
	Total	1.87	0.72	0.06	1.76	1.99	0.48	4.6	
AVR U/A	Control	1.42	0.33	0.04	1.35	1.50	0.64	2.02	
	Cases	2.3	0.45	0.05	2.16	2.37	2.3	4.1	<0.001
	Total	1.84	0.58	0.05	1.75	1.94	0.64	4.1	

Figure –17 shows Doppler clinical variables in the study group. The mean average of both right and left uterine Doppler in the control group is 1.42 with its minimum of 0.64 and maximum of 2.02.In the case group with mean average of 2.3 with its minimum of 2.3 and maximum of 4.1.

Table – 13 Number of women in case and control group started on prophylactic aspirin

Aspirin	Control	(%)	Cases	(%)
Started	1	1%	23	31%
Not Started	74	99%	52	69%
Total	75		75	

Figure – 18 Number of women in case and control group started on prophylactic aspirin
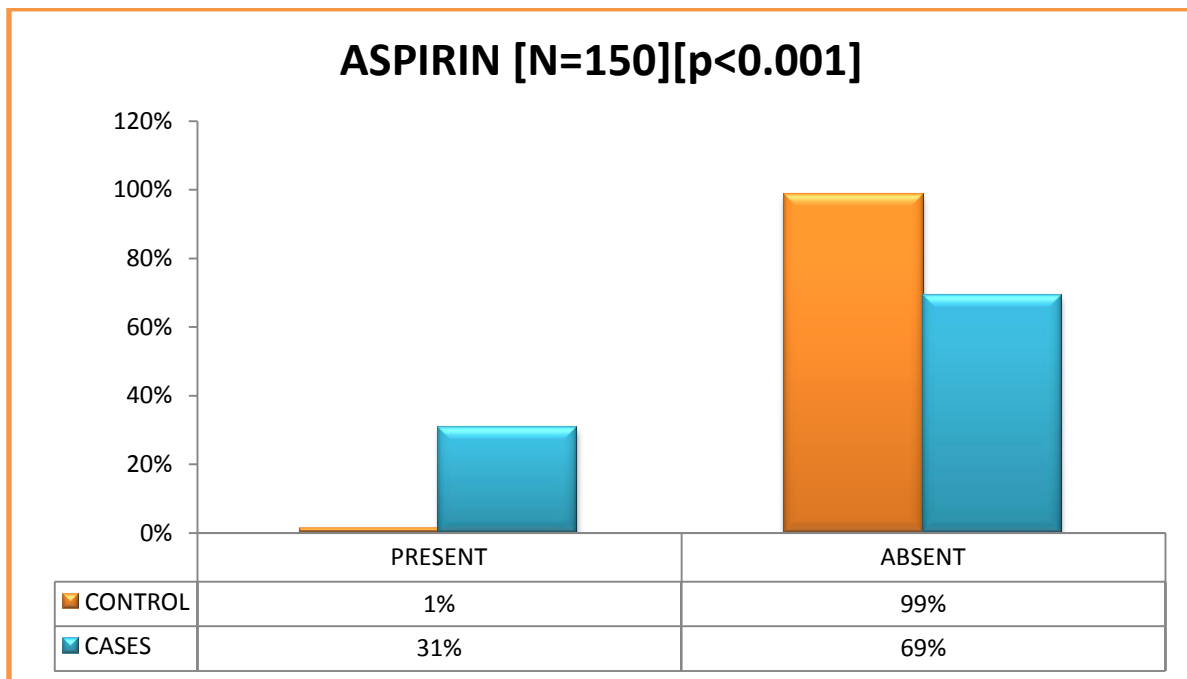
Table – 13 and figure -18- shows that 1% in control group was started on aspirin in view of age > 30years. In case group 31% were started on aspirin in view of average uterine artery PI more than 95th percentile(> 2.3).

Table –14 Association of 2rd trimester abnormality in both group

Table –14 Association of 2rd trimester abnormality in both group

2 - Doppler	Control	(%)	Cases	(%)
NORMAL	71	95%	65	87%
RT-DN+	0	0%	3	4%
LT - D N +	0	0%	4	5%
B/L UA N+	1	1%	0	0%
QUIT	3	4%	3	4%
TOTAL	75		75	

Figure –19 Association of 2rd Trimester Doppler abnormality in both group

2 - DOPPLER [N=150][p>0.05]

	NORMAL	RT-DN+	LT - D N +	B/L UA N+
CONTROL	95%	0%	0%	1%
CASES	87%	4%	5%	0%
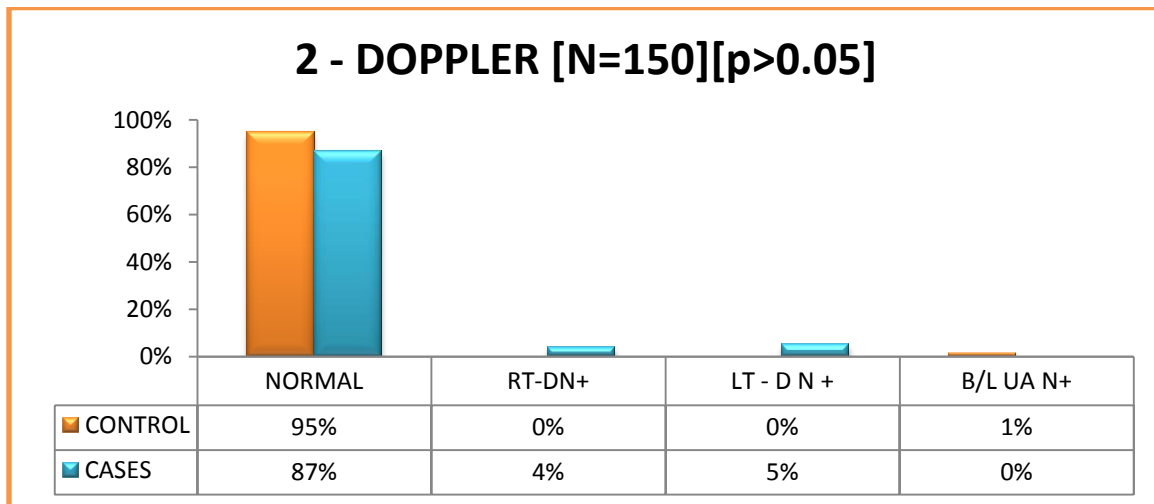
Table -14 and Figure -19 - Shows association of 2nd trimester Doppler with study group. In the control group 71 of had normal dopplers and 1 had bilateral uterine artery Doppler notching. Remaining 3 was quit after 1st trimester scan. In the case group 65 of them had normal Doppler and 3 & 4 (total 7) had right and left uterine artery diastolic notching. Out of 7 / 5 were started on prophylactic aspirin in the first trimester and 3 of them ended up in having pre-eclampsia. As compared to comtrol group, there are 2nd trimester Doppler abnormality in women who had their 1st trimester Doppler abnormality.Of which 50 % of them ending up in adverse pregnancy outcome.

Table – 15- Association of 3rd Trimester Doppler abnormality in both group

3 - Doppler	Control	(%)	Cases	(%)
NORMAL	68	91%	67	89%
ABNORMAL	1	1%	2	3%
QUIT	6	8%	6	8%
Total	75		75	

Figure –20 Association of 3rd Trimester Doppler abnormality in both group

3rd Trimster Doppler Abnormality [N=150][p>0.05]

	NORMAL	ABNORMAL	QUIT
CONTROL	91%	1%	8%
CASES	89%	3%	8%
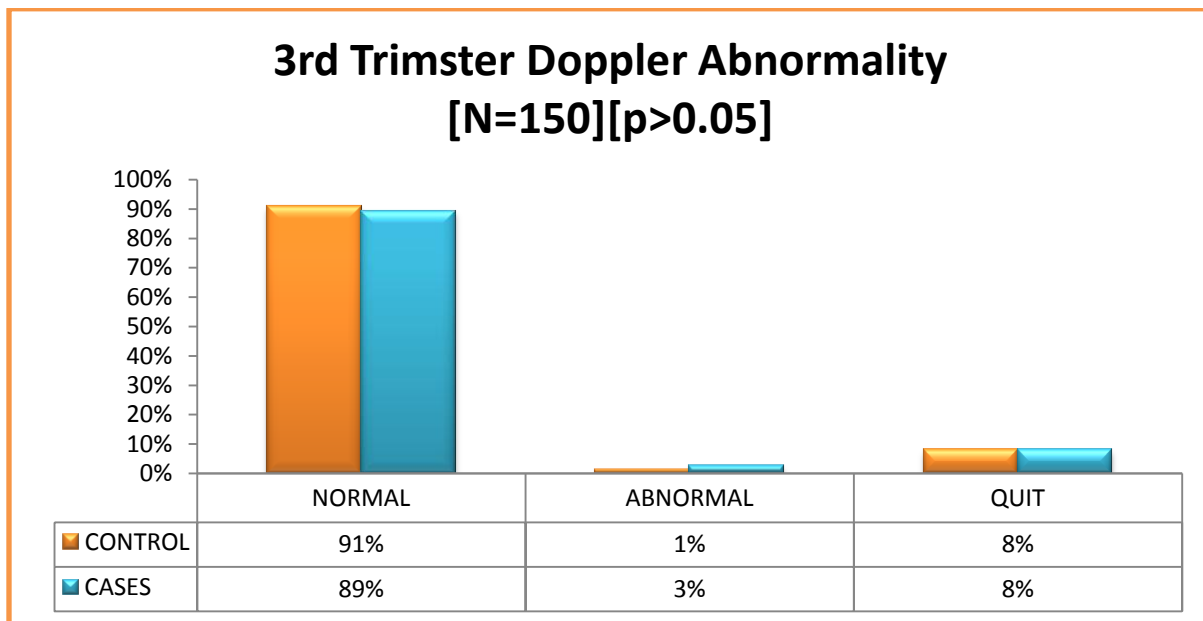
Table –15 and Figure – 20 Shows Third trimester Doppler abnormality was about 1% in control and 3% in the case group. There is no significant difference in both the groups

Table - 16   Shows association of IUGR with study group

IUGR	Control	(%)	Cases	(%)
PRESENT	4	5%	21	28%
ABSENT	71	95%	54	72%
Total	75		75	

Figure -21 Shows association of IUGR with study group
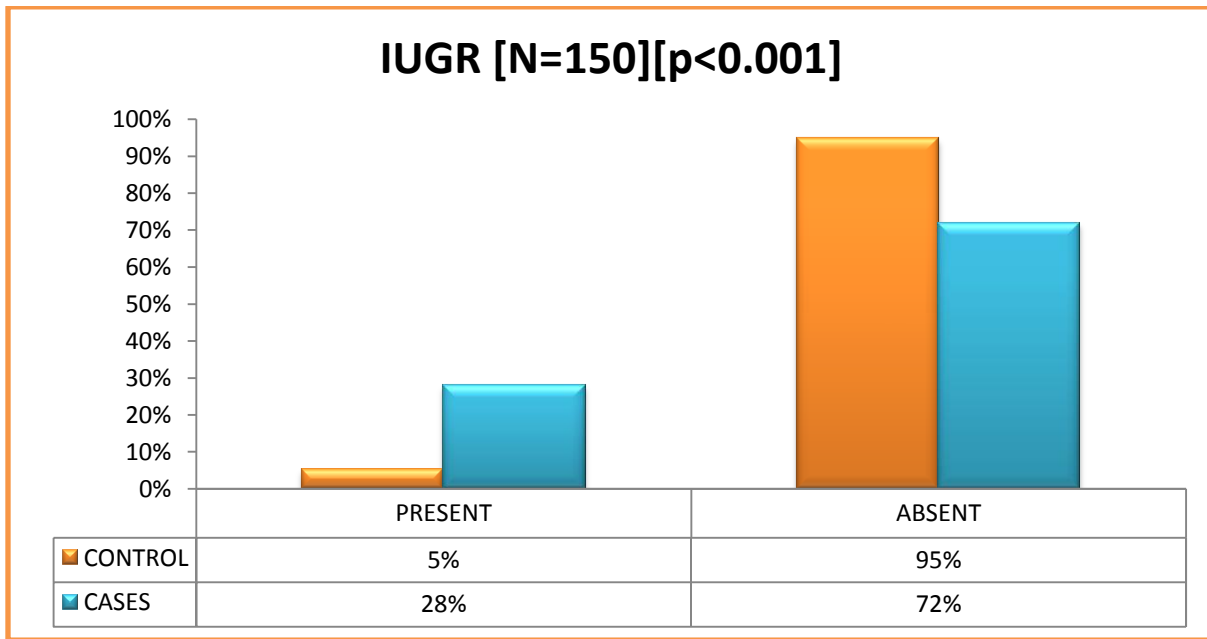
Table -16 and Figure - 21 Shows association of IUGR in the study group.In the control group5% of them had IUGR and in the case group 28% of them had IUGR . This shows that there is significant outcome in the case group than control group. There are significant cases of IUGR in case group for both average and single uterine artery PI ≥ 2.3.

Table – 17 Shows association of Oligohydramnios in the study group

OLIGO	Control	(%)	Cases	(%)
PRESENT	5	7%	8	11%
ABSENT	70	93%	67	89%
Total	75		75	

Figure - 22 Shows association of Oligohydramnios in the study group

	PRESENT	ABSENT
CONTROL	7%	93%
CASES	11%	89%

OLIGO [N=150][p>0.05]
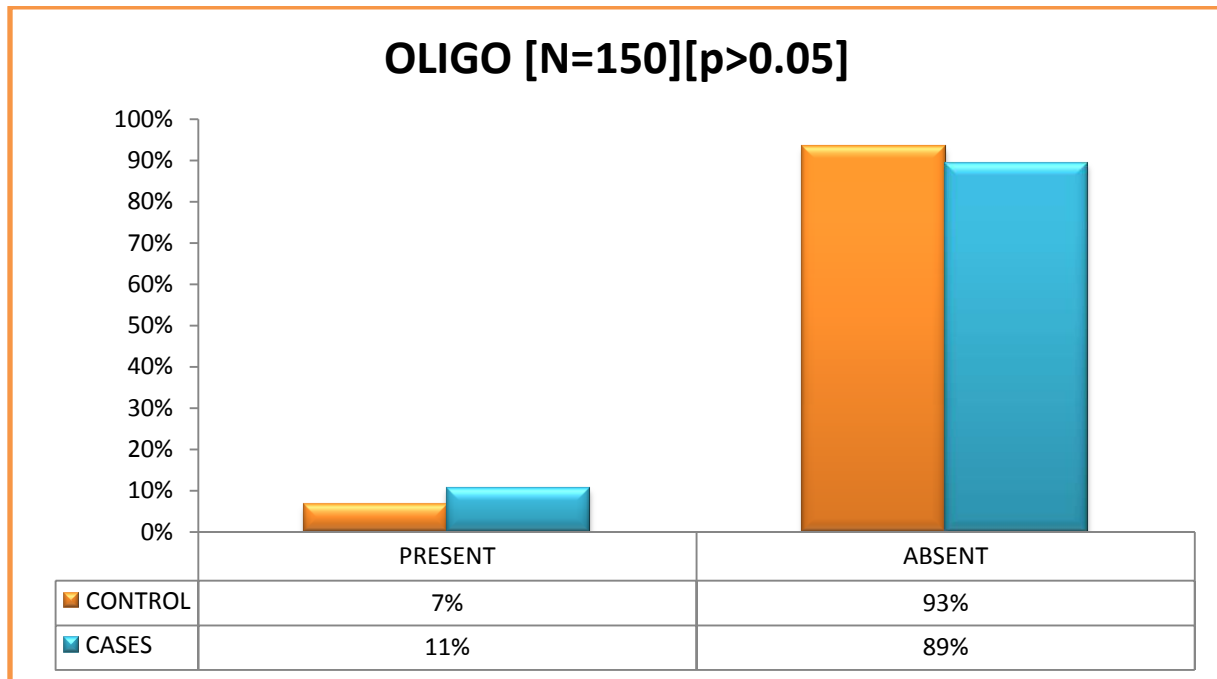
Table –17 and Figure –22 shows association of Oligohydramnios in the study groups .In the control group 7% of them had oligohydramnios and in the case group 11% of them had oligohydramnios.There is no significant outcome between these groups.

Table –18 Shows association of Gestational Hypertension with the study group

G.HTN	Control	(%)	Cases	(%)
PRESENT	1	1%	4	5%
ABSENT	74	99%	71	95%
Total	75		75	

Figure –23 Shows association of Gestational Hypertension with the study group
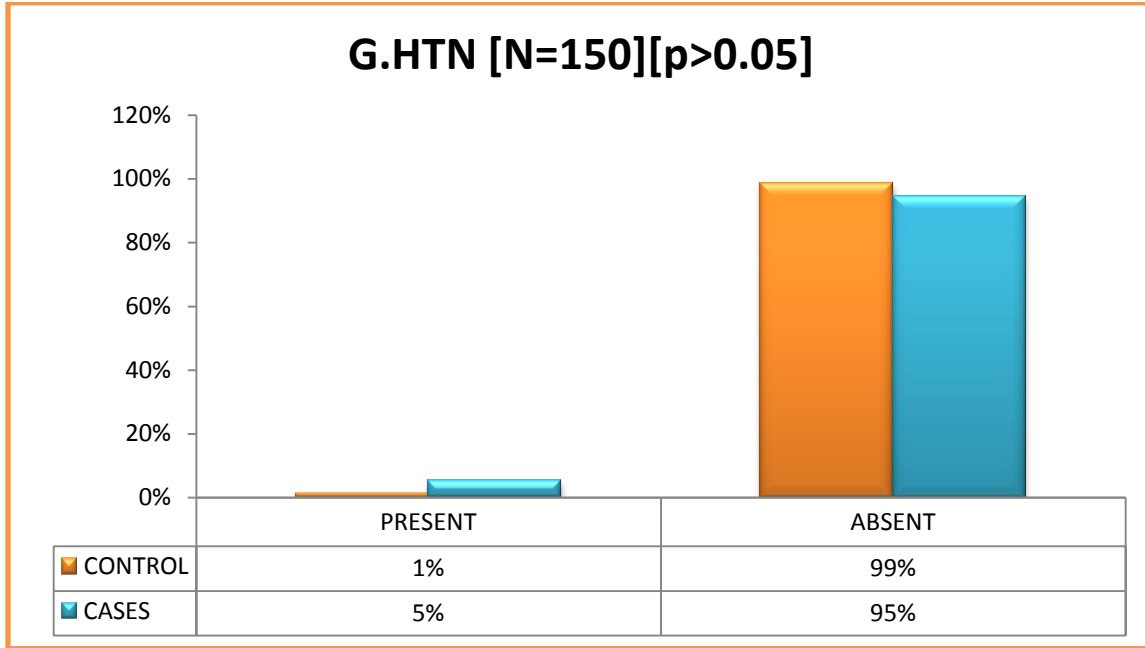
Table –18 and Figure- 23 shows association of Gestational Hypertension in the study groups. In the control group 1% and in the case group 5% of them had Gestational Hypertension.. Out of 4, 3 had average uterine artery Doppler more than 2.3(maximum of 2.7) and 1 had single uterine artery Doppler abnormality. None of the 4 were started on prophylactic aspirin.

Table –19 Shows association of Pre-eclampsia in the study groups

PRE -ECL	CONTROL	(%)	CASES	(%)
PRESENT	0	0%	6	8%
ABSENT	75	100%	69	92%
Total	75		75	

Figure –24 Shows association of Pre – eclampsia in the study groups
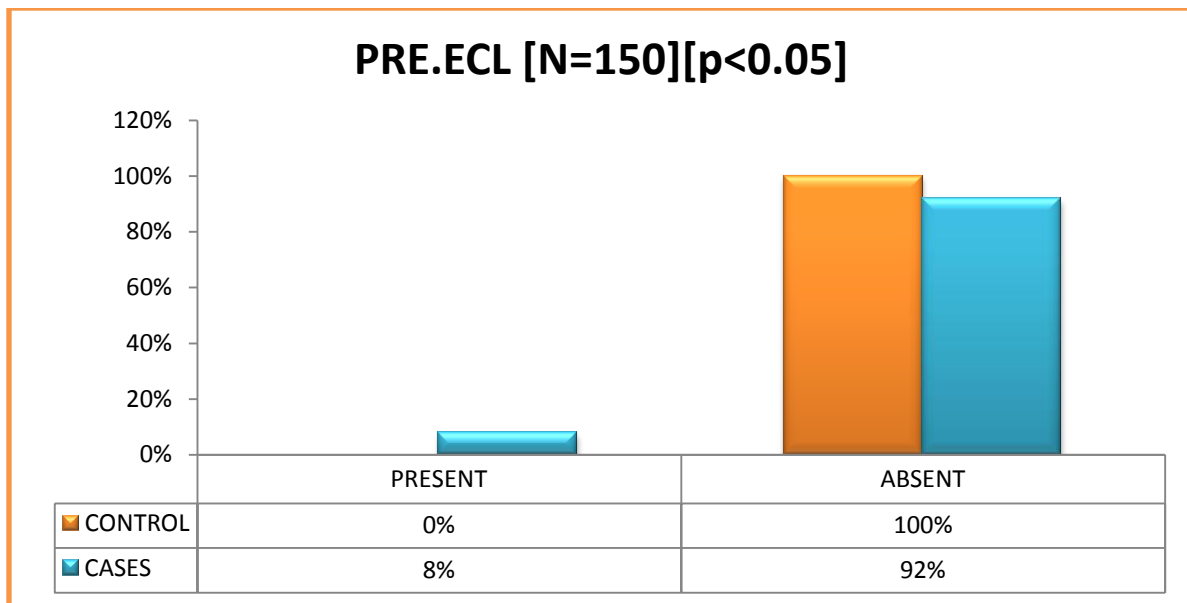
Table –19 and Figure -24 shows association of Pre – eclampsia in the study group. In the control group none of them had pre – eclampsia. In the case group 8% of them had preeclampsia and none in the control group had PE.Out of 6 , 5 were started on prophylactic aspirin in the first trimester for abnormal Doppler and 1 was not started on aspirin. There is significant outcome in the case group as compared to the control group. Role of aspirin in the prevention of preeclampsia was not much effective. Out of 6, 4 had average uterine artery PI > 2.3 and 2 had single uterine artery PI > 2.3.

Table – 20 Shows the Abnormal uterine Doppler in the case group and adverse pregnancy outcome

Clinical Variables	Total	IUGR	OLIGO	G+HTN	PE	Eclampsia
Single Uterine Artery Doppler [Right/Left] with its PI >/=2.3	42	10	3	1	2	0
	56%	**13%**	**4%**	**1%**	**3%**	**0%**
Average of Right and Left Uterine Artery Doppler with its PI >/=2.3	33	11	5	3	4	0
	44%	**15%**	**7%**	**4%**	**5%**	**0%**
Total	75	21	8	4	6	0
(%)	**100%**	**28%**	**11%**	**5%**	**8%**	**0%**

Table – 20 Shows the abnormal uterine artery Doppler in the study group and adverse pregnancy outcome. Out of 75 in the case group, Single uterine artery Doppler abnormality was found in 42 and 33 are with average uterine artery Doppler $\geq$2.3. Both of them are associated with adverse pregnancy outcome (average PI >2.3 is slightly more than single PI >2.3).

Figure-25 Shows abnormal uterine Doppler in the case group and adverse pregnancy outcome
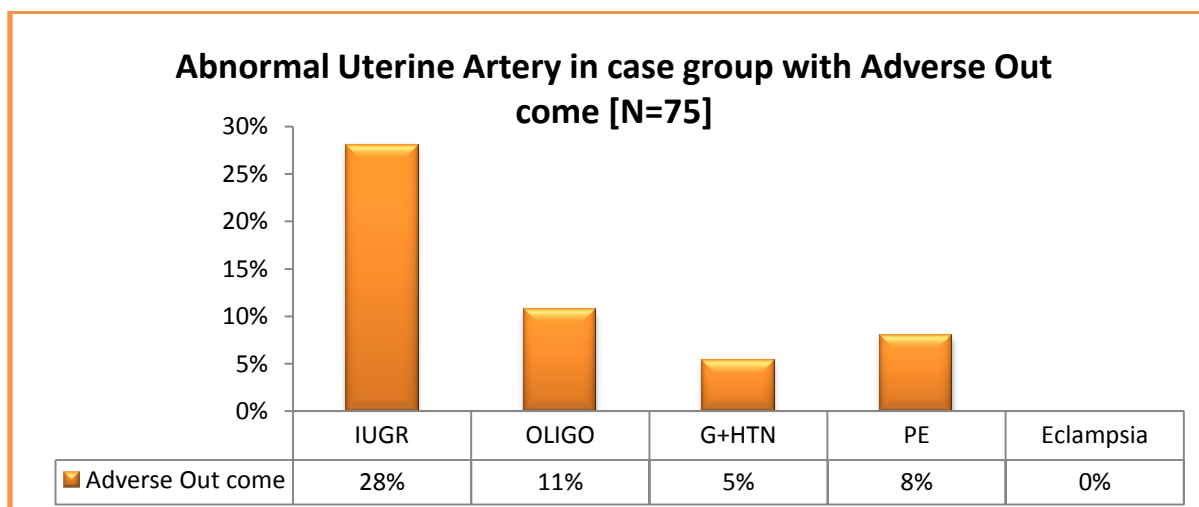
In the case group the maximum % of adverse pregnancy outcome is with IUGR – 28% and least % for G.HTN – 5% and 0% outcome with eclampsia.

Table – 21 Shows various adverse pregnancy outcome in both control and case group

Clinical Variables	Control	Cases	Sig
IUGR	6%	28%	<0.001
OLIGO	7%	11%	>0.05
G.HTN	1%	5%	>0.05
PRE ECL	0%	8%	>0.05

Figure –26 Shows overall prevalence of adverse pregnancy outcome in the case group
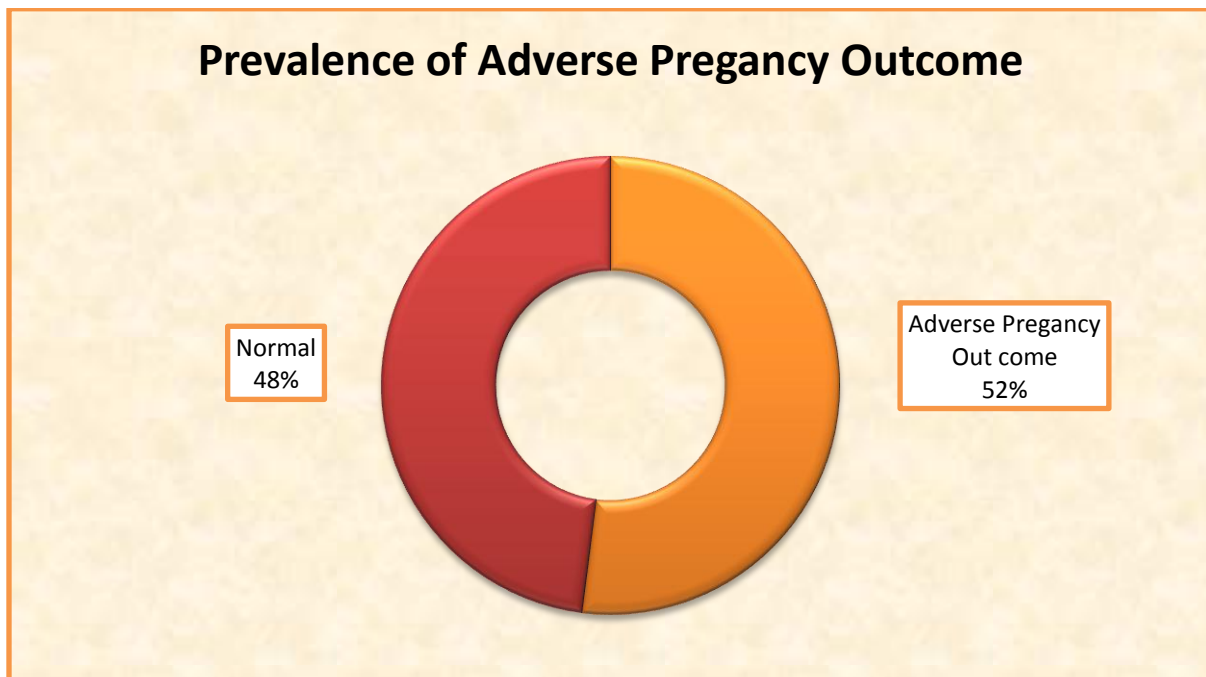
Table –21   and Figure -26 shows the prevalence of adverse pregnancy outcome in the case group. In the case group the adverse pregnancy outcome was associated with 52 % and 48% is normal .Adverse pregnancy outcomes such as IUGR, Oligohydramnios, G.HTN and Preeclampsia are included in the study.

Figure –27 Association of adverse pregnancy outcome in the study groups

Assoication of Adverse Pregancy Outcome with Study Group [N=75][p<0.001]

	CONTROL	CASE
Adverse Outcome	19%	52%
Unaffected	81%	48%
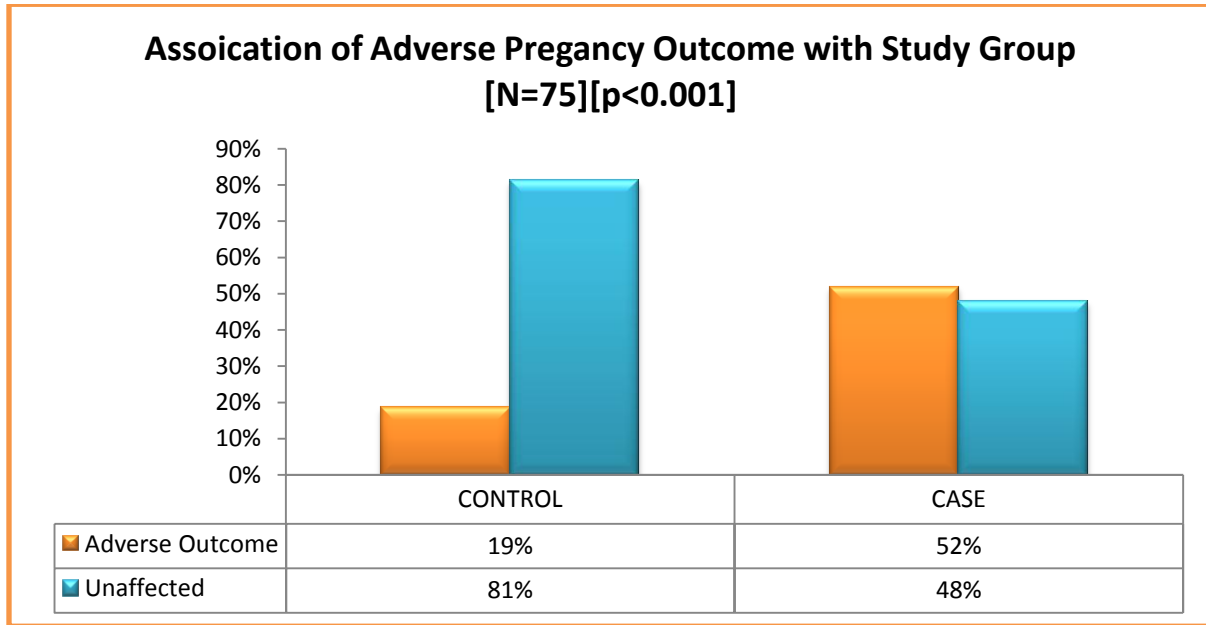
In the case group 52% are associated with adverse pregnancy outcome , but in the control group only 19% were associated with adverse pregnancy outcome. Adverse pregnancy outcome which were included are IUGR, Oligohydramnios , G.HTN, preeclampsia and Eclampsia.So there is significant outcome in the case group as compared to control group.The P value is highly significant.

Table – 22 Shows gestational age at which the pregnancies were terminated in both the groups

GA (weeks)	Control	(%)	Cases	(%)
<37 weeks	3	4%	12	16%
> 37 weeks	62	83%	49	65%
QUIT	10	13%	14	19%
Total	75		75	

Figure –28 Shows the gestational age at which the pregnancies were ended in both the groups

GA (weeks) [N=150][p<0.05]

	< 37 weeks	> 37 weeks	QUIT
CONTROL	4%	83%	13%
CASES	16%	65%	19%
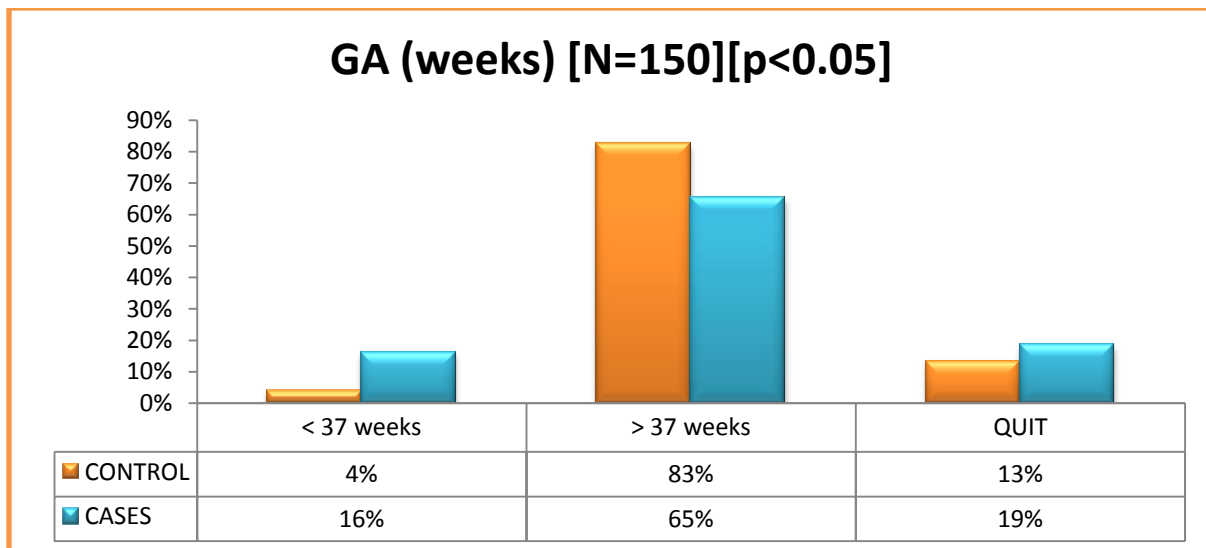
Table –22 and figure-28 shows the gestational age at which the pregnancies were terminated. In the control group 3 had their delivery < 37weeks in view of preterm labour(2) and PPROM(1) ,remaining are > 37weeks. In the case group 12 of them had their deliveries <37 weeks

Table –23 Pregnancy terminated in case & control gp <37weeks

Pregancy Terminated	Case	(%)	Control	(%)
S.PRE ECLAMSIA	4	5%	0	0%
G.HTN	3	4%	0	0%
G.HTN+IUGR	1	1%	0	0%
S.OLIGO DRAMNIOVS	1	1%	2	3%
S.IUGR	3	4%	1	1%

3 had preterm labour. The lowest gestational age in the case group at which the pregnancy terminated was 33 weeks for severe preeclampsia.

Figure – 29 Pregnancy terminated in case and control group

CONTROL [N=75]

IUGR 1%

Spontaneous Preterm 4%

Oligo 3%

Quit 13%

Normal 79%
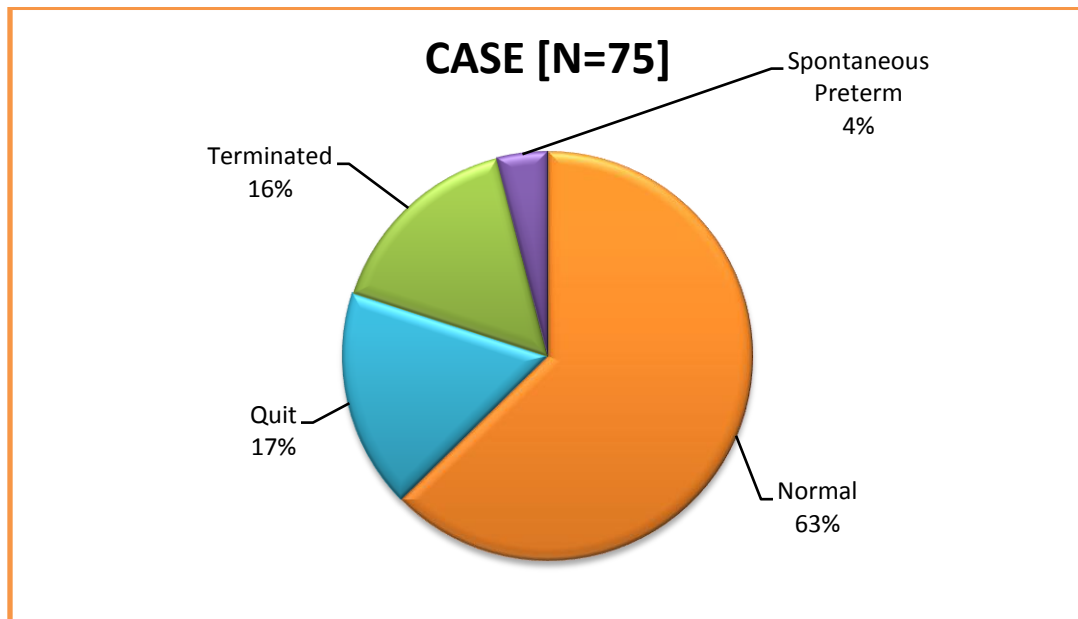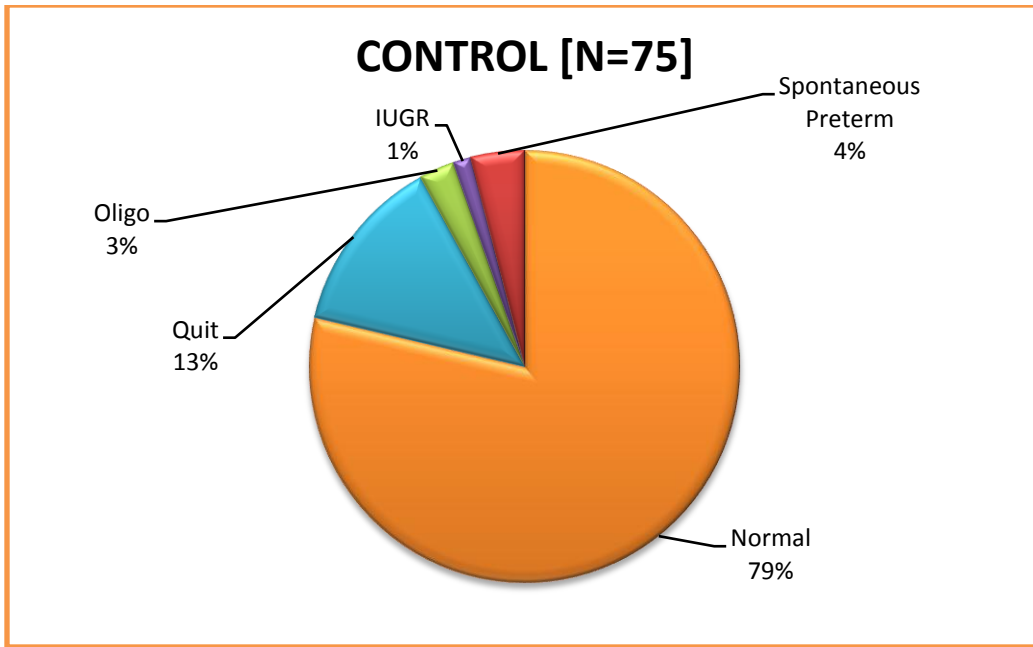
Patients in the case group has been more induced than in the control group.

Table – 24 Shows the range of birth weight in both control and case group

Birth weight(kg)	Control	(%)	Cases	(%)
< 2.0	0	0%	5	7%
2.01 - 2.50	4	5%	16	21%
2.51 - 3.50	50	67%	38	51%
> 3.50	11	15%	2	3%
Quit	10	13%	14	19%
Total	75		75	

Table – 25 Shows the mean birthweights(kgs) with the study groups

Birth weight [Kgs]	Mean	SD	Std. Error	95% CI for Mean		Minimum	Maximum	Sig
				Lower	Upper			
CONTROL	3.056	0.42591	0.05283	2.9505	3.1615	2.03	3.91	<0.001
CASES	2.7329	0.52075	0.06614	2.6007	2.8651	1.34	3.75	

Table 24 and 25 - shows the mean birth weight in the study group. The mean birth weight in the control group was 3.056kg with minimum birth weight of 2.03kg and maximum weight of 3.9kg. In the case group the mean birthweight was 2.7kg with minimum birthweight of 1.34kg and maximum weight of 3.75kg.

Table –26 Association of mode of deliveries with the study groups

Mode of Deliveies	Control	(%)	Cases	(%)
Elective LSCS	5	7%	6	8%
Emergency LSCS	16	21%	12	16%
NVD	33	44%	35	47%
VAVD	11	15%	8	11%
Quit	10	13%	14	19%
Total	75		75	

Figure –30 Shows association of mode of deliveries with the study groups.
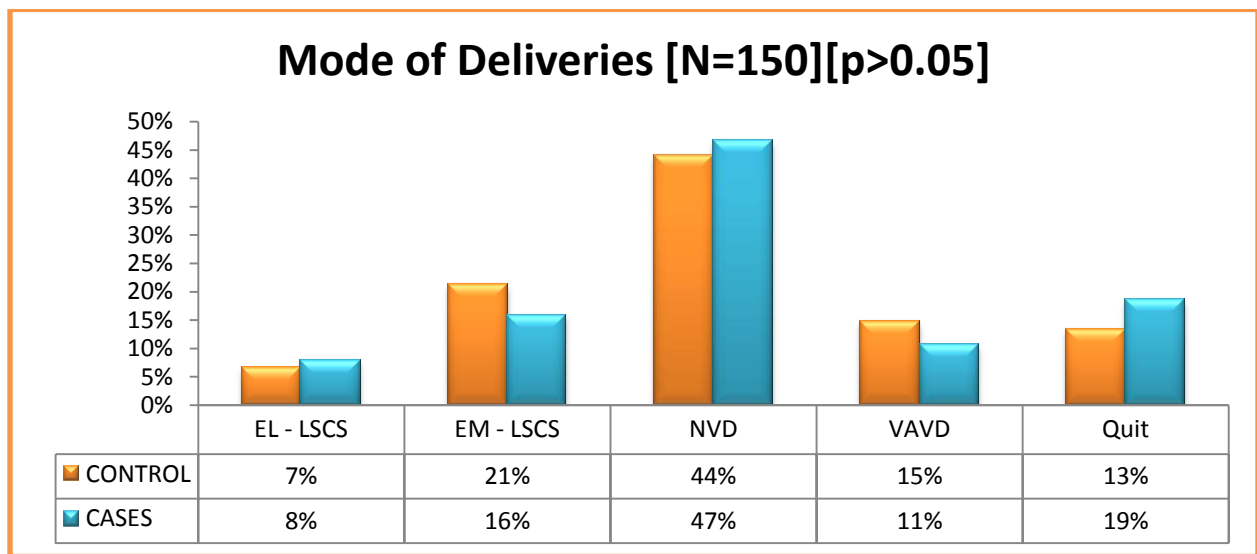
Table- 26 and Figure -30 shows association of mode of deliveries with the study groups. Of the total study group 9% of them have undergone elective c- section for primigravida with breech presentation and repeat lscs with history of previous lscs, 23% of have undergone emergency lscs for obstetrical indications. 54% delivered normally and 15% by vaccum assisted delivery.

Table –27 Summary of all Clinical variables in the study group

Comparison of cases and control subjects			
Clinical Variables	**Control**	**Cases**	**Sig**
AGE			
Mean +/-SD	25.2+/-3.5	26.1+/-3.9	>0.05
PARITY			
PRIMI	51%		>0.05
MULTI	49%		
FAMILY HISTORY	7%	19%	<0.05
PREVIOUS OBSTERTRIC HISTORY			
BOH	1%	5%	
PE	0%	1%	>0.05
NIL	99%	93%	
MEDICAL HISTORY	13%	19%	>0.05
U/A L			
Mean +/-SD	1.4+/-0.41	2.26+/-0.65	<0.001
U/A R			
Mean +/-SD	1.4+/-0.41	2.26+/-0.65	<0.001
AVR U/A			
Mean +/-SD	1.42+/-0.33	2.26+/-0.45	<0.001
Pregancy Out come	19%	52%	<0.001
GA (weeks)			
< 37 weeks	5%	20%	
> 37 weeks	95%	80%	<0.05
PREGANCY TERMINATED	4%	16%	>0.05
MODE OF DELIVEIES			
EL - LSCS	8%	10%	
EM - LSCS	25%	21%	
NVD	51%	56%	
VAVD	17%	13%	>0.05
BIRTH WEIGHT [kgs]			
Mean +/-SD	3.06+/-0.43	2.73+/-0.53	<0.001

Data Analysis - Methods:

The data are reported as the mean +/- SD or the median, depending on their distribution. The differences in quantitative variables between groups were assessed by means of the unpaired 't' test. Comparison between groups was made by the Non parameteric Mann - Whitney test.

The chi square test was used assess differences in categoric variables between groups. A p value of <0.05 using a two-tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package. (SPSS, version 16.0 for windows)

DISCUSSION

Hypertensive disorders of pregnancy are one of the most common complications of pregnancy with the incidence of 5 -10%. The associated maternal morbidity, mortality and neonatal complications are very adverse indicating the need for early identification of the condition preferably before onset of clinical disease. Lot of research has been done and many screening options are identified for predicting development of hypertensive disorders in pregnancy. But no single screening test is useful.

Many studies done in second trimester investigated the value of uterine artery Doppler in prediction of development of hypertensive disorders of pregnancy, scientific interest is now focused on first trimester. This gives the opportunity of early intervention for modifying the severity of the disease and meticulous surveillance for early identification of the disease.

This is a prospective study conducted at the Department of Obstetrics and Gynaecology at PSG Institute of Medical science and Research centre, Peelamedu, Coimbatore between January 2016 – January 2017 with the aim to evaluate the predictive value of first trimester uterine Doppler for development of adverse pregnancy outcome..

In this study 150 women, representative of local pregnant population irrespective of parity are recruited with follow up rate of 100%.

All the antenatal mothers attending the OPD between 11 – 13weeks + 6days are chosen to perform uterine artery Doppler because a routine NT scan is scheduled in the study population at this time of gestation. Based on the uterine Doppler value, my study population (n – 150) is divided equally (each 75) into control and case group. In the case group uterine artery Doppler value, both single uterine artery Doppler and average uterine Doppler $\geq$ 2.3 is considered as

abnormal and Doppler ≤ 2.2 is considered as control group(normal). Abnormal dopplers in the case and normal dopplers in the control group was followed up for development of adverse pregnancy outcome till delivery. All pregnant women were screened for risk factors such as previous obstetric history of preeclampsia, family history of hypertension / diabetes, h/o chronic hypertension.

Uterine artery Doppler indices – Pulsality Index in the first trimester is considered abnormal, when PI is ≥ 2.3 in both average and single uterine artery Doppler. The exclusion criteria were (1) Chronic hypertension (2) Twins (3)Missed abortion (4) Not consenting.

Once the abnormal dopplers were found, the patients were closely followed up during every antenatal visit for the development of G.HTN, PE , IUGR & Oligohydramnios. They have been monitored for the development of abnormality in the 2nd and 3rd trimester dopplers. Both case and control group had the same follow up irrespective of normal Doppler values in the control group.

In my study population out of 150 patients studied, 43% were between 21 – 25 yrs of age and 37% were between 26 – 30 yrs of age. There is no significant difference between both the groups.

In my study population (150 no's) maximum women i.e 54% are primigravida . Youngest primi being 18 years and eldest primi is 35 years old. 46% are multigravida, youngest multigravida is 21 years and eldest multigravida is 39 years old.

In the family history about 7% and 19% of women in control and cases group have significant family history. Family history of Diabetes Mellitus(DM), Hypertension(HTN), DM

and HTN included in this. There is no significant family history of preeclampsia or eclampsia found in these groups. Family history is insignificant in my study group for adverse pregnancy outcome.

Medical history in the study population such as overt hypothyroid, Type 2 DM, GDM OHA. In case group ,1 patient with history of chronic hypertension present. There is no significant difference in the case and control group with the medical history.

In the study group ,1% in the control group and 5% in the case group has BOH due to 2 Neonatal death and 2 term IUD. Among them none of have developed hypertensive disorder of pregnancy. One of them was diagnosed to have APLA +ve preconceptionally ,for which she was started prophylactically on aspirin and heparin.

Uterine artery Doppler variables in the study population is divided based on the abnormality as control and case group. Doppler value in the control group is considered when it is $\leq$ 2.2 and Doppler value in the case group is considered when it is $\geq$ 2.3 (abnormal) for both single and average uterine artery Doppler.

In the study population those who had abnormal uterine Doppler ($\geq$ 2.3) was started prophylactically on aspirin.1% in control group was started on aspirin in view of age > 30years. In case group 31% were started on aspirin in view of average uterine artery PI more than 95th percentile ($\geq$ 2.3).

Follow up of study group for Doppler abnormality in the 2nd and 3rd trimester were carried out. There was no significant finding in both control and case group.

My study population was followed up for the development of adverse pregnancy outcome till delivry such as G.HTN, PE, Oligohydramnios and IUGR. 52% in the case group and 19% in the control group were associated with adverse pregnancy outcome. More % of adverse outcome in the case group is for IUGR as compared to other variables.

Gestational age at which pregnancies were terminated are analysed . In the control group 3 had their delivery < 37weeks in view of preterm labour(2) and PPROM(1) ,remaining delivered ≥ 37weeks. In the case group 12 of them had their deliveries <37 weeks in view of severe PE (4), G.HTN (3), G.HTN+IUGR(1), Severe .IUGR(3), Severe Oligohydramnios(1).

Birth weight in the study was analysed in both groups. These groups were categorized as very low birthweight(<2kg), low birth weight(2-2.5kg) and normal(>2.5).In the control group 5% of them had low birth weight and 95% had normal birthweight. In the case group 7% had very low birth weight, 21% had low birth weight and 72% of them had normal birthweight.

Of the total study group 9% of them have undergone elective c- section for primigravida with breech presentation and repeat lscs with history of previous lscs, 23% of have undergone emergency lscs for obstetrical indications. 54% delivered normally and 15% by vaccum assisted delivery.

Age distribution and parity index were analysed for association of adverse pregnancy in the case group. It is evident from the observation that most of the adverse pregnancy outcome is for reproductive age group between 21-30 years and adverse outcome was more for the primigravida in my study population. It is consistent with the study done by Parra-codero M et al,[105] 51% of primigravida developed hypertensive disorders of pregnancy. This shows that

nulliparous women who are exposed to paternal antigen for the first time are at increased risk of developing hypertensive disorders of pregnancy.

Other parameters such as family history, previous obstetric history, medical history was not significant in my study population. These parameters are considered in my study population as reference to the following study - Plasencia et al,[85] investigated the performance of screening for PE using maternal characteristics such as body mass index, age, ethnic origin, smoking, medical and obstetric history and uterine artery PI in the first trimester. They concluded that in unaffected individuals log MoM PI was influenced by maternal ethnic origin, body mass index, previous history of PE and fetal crown-rump length. In the prediction of PE significant contributions were provided by log MoM PI, ethnic origin, body mass index and previous and family history of PE. They also added that for a false-positive rate of 10% the predicted detection rate of PE requiring delivery before 34 weeks was 82%, compared to 31% for late PE, 12% for gestational hypertension and 18% for small for gestational age.But this is contradictory to my study.

In the present study, abnormal uterine artery Doppler indices(> 95th percentile) noted in 11 - 13w+6days are compared for their predictive values in the development of adverse pregnancy outcome , such as development of gestational hypertension, PE, eclampsia, IUGR and oligohydramnios in the study population and with the available studies which are a few in first trimester.

Abnormal Doppler value $\geq$ 2.3(>95th percentile) is taken as cut off as reference to this study. In the study conducted by Gomez et al,[65] where 999 pregnant women were examined between 11 to 14 weeks during routine scan using transvaginal color and pulsed Doppler. The

authors found a significant change in the 95th percentile of mean uterine artery PI with advancing gestation. They reported a progressive decrease in the prevalence of bilateral notching and PI with gestation. There were 22 cases of PE, and using a cut-off of PI above the 95th percentile, the sensitivity, specificity, PPV and NPV were 245, 95.1%, 11.3% and 97.9% respectively. The authors of the study acknowledged the potential advantages of early screening for PE and associated complications, but concluded that there is a limited role for uterine Doppler velocimetry in identifying the pregnancies with increased risk of developing hypertensive disorders.

In the case group out of 75, 56% of them had single uterine artery Doppler(SUAD) PI > 2.3 and 44% with average uterine artery Doppler (AUAD) PI >2.3.Out of 56% in the SUAD 38% had adverse pregnancy outcome and out of 44% with AUAD 69.6% had adverse pregnancy outcome. In both the groups the maximum adverse outcome was with IUGR.

Control group has 19% adverse pregnancy outcome, 6% for IUGR, 7% for oligohydramnios, 1% fot G.HTN and 0% for PE. Case group has 52% of them had adverse pregnancy outcome, 28% for IUGR, 11% for oligohydramnios, 5% for G.HTN, 8% for PE. P value is highly significant (<0.001) with case group as compared to control group for adverse pregnancy outcome.

Thus as compared to control group , case group has significant adverse pregnancy outcome

On total of the case group 52% of the population has adverse pregnancy outcome in my study population. Both average and single uterine artery Doppler $\geq$2.3 is significant from my study, but average is more significant than single uterine artery Doppler. There were no cases of Eclampsia noted in my study population.

- There was no studies found which is consistent with single uterine Doppler abnormality and adverse pregnancy outcome. The results of which is from my study population.Thus i conclude from above that measuring single uterine artery Doppler is also found to be significant even if the average is ≤ 2.3.

- In summary, first trimester uterine artery Doppler in predicting adverse pregnancy outcome has advantages such as easily measurable, non invasive , done along with NT scan, can be started on prophylactic Loprin, which has some preventive role in adverse pregnancy outcome. Close monitoring of these patients result in early diagnosis, thus it reduces both maternal and perinatal mortality and morbidity. Thus above finding suggest that adding first trimester uterine artery Doppler to NT scan has great advantage in predicting adverse pregnancy outcome.

CONCLUSION

In pregnancy, hypertensive disorders are major cause for maternal and perinatal morbidity and mortality worldwide, particularly in developing countries than developed countries. Since, its etiology remains unknown, and there is no effective treatment for this complication, the identification of women who are at risk of developing will be of great value. This will help us to find women who require close antenatal surveillance, allow early referral for timely delivery, when signs or symptoms occur.

Over the span of 12 months , antenatal mothers coming to the OPD at PSG IMSR were screened for abnormal uterine artery Doppler and those who had abnormal dopplers were closely monitored for the development of adverse pregnancy outcome. This early identification of high risk women can be helpful for us to start them with prophylactic aspirin which may help in modifying disease severity and time of disease occurrence.

Out of 150 women recuited in the study, 75 each has been divided between case and control group. In the case group, out of 75, 56% of them had their single uterine artery Doppler adnormality with adverse pregnancy outcome of 38%.Remaining 44% had their average uterine artery Doppler PI abnormality, out of which 69.6% of them had adverse pregnancy outcome.The maximum adverse outcome of my study population is with IUGR.

The study showed that first trimester uterine artery Doppler with single and average uterine artery PI >95th centile(2.3) has better screening value in my population.

The overall performance of the first trimester uterine artery Doppler in the prediction of adverse pregnancy outcome is valuable.

The sensitivity of first trimester uterine artery Doppler can be improved by doing combined screening with the maternal characteristics in addition to Doppler changes.

By identifying the high risk women who has high predictive value for the development for adverse pregnancy outcome are closely monitored. Thus it has reduced the incidence of maternal and perinatal morbidity and mortality.

This can be further improved by addition of other parameters like biochemical markers.

To conclude from the present study, first trimester Doppler ultrasound is the best non-invasive investigation to assess changes in uteroplacental hemodynamics which helps in early prediction of development of hypertensive disorders in pregnancy along with maternal characteristics which helps in early prophylactic intervention.

Further research is required to evaluate the generalizability of multiparametric models in different resource settings, in addition to assessing the impact of screening on clinical outcomes.

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December 9, 2016

To
Dr Arivarasi Sai Gokull Raj
Postgraduate
Department of Obstetrics & Gynaecology
Guide: Dr K Balasudha
PSG IMS & R
Coimbatore

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore - 4, has reviewed your proposal on 9th December 2016 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your request to renew the approval for the study entitled:

"First trimester uterine artery doppler (11-13w+6 days) in prediction of adverse pregnancy outcome"

The following documents were received for review:

1. Request for renewal dated 03.12.2016
2. Status Report

After due consideration, the Committee has decided to renew the approval for the above study.

The members who attended the meeting held on at which your proposal was discussed, are listed below:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr D Vijaya	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The approval is valid for one year (30.12.2016 to 29.12.2017).

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Yours truly,

Dr S Bhuvaneshwari
Member – Secretary
Institutional Human Ethics Committee

Proposal No. 15/403

INFORMED CONSENT

PSG Institute of Medical Science and Research, Coimbatore

Institutional Human Ethics Committee

INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I , DR . ARIVARASI SAI GOKULL RAJ, am carrying out a study on the topic:

UTERINE ARTERY DOPPLER IN FIRST TRIMEATER (11-13+6WKS) IN PREDICTION OF ADVERSE PREGNANCY OUTCOME

as part of my research project being carried out under the aegis of the Department of :

OBSTETRICS AND GYNAECOLOGY, PSG IMSR

My research guide is: DR. BALASUDHA ,, D.G.O.,DNB,Professor IN Dept of OBG

The justification for this study is:

Uterine artery Doppler Waveform analysis has been extensively studied in the second trimester of pregnancy as a predictive marker for the late development of pre eclampsia , placental abruption and fetal growth restriction.The use of Doppler interrogation of the vessel in the first trimester has gained momentum in identifying the early onset than late onset pre eclampsia.

The objectives of this study are:

Correlation of Uterine Artery Doppler in the First Trimester with Adverse pregnancy Outcome.

Sample size: 150 no's

Study volunteers / participants are (specify population group & age group): Antenatal patients with single pregnancy

Location: OBG OPD ,PSG IMSR,COIMBATORE

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration):___10__ minutes.

Data collected will be stored for a period of __5_ years. We will / will not use the data as part of another study.

Final interview ___10_ mts.

Benefits from this study:

   1))   Early prediction of later pregnancy outcomes which initiates the early management strategies that may

       prevent or mitigate theses complications.

   2) To plan for the timing of delivery

Risks involved by participating in this study: NIL

How the **results** will be used: Can show positive correlation or negative correlation.

  From this we ll able to find the Cut off value of Uterine artery Doppler at first trimester in early prediction of adverse pregnancy outcome

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be

used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 9585093324

Contact number of Ethics Committee Office: During Office hours: 0422 2570170 Extn.: 5818

                                                            After Office hours: 9865561463

பூ. சா. கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

மனித நெறிமுறைக் குழு

ஒப்புதல் படிவம்

தேதி:

மரு. அறிவரசி சாய் கோகுல் ராஜ், ஆகிய நான் பூ. சா. கோ மருத்துவக் கல்லூரியின் / மருத்துவமனையின் மகப்பேறு மற்றும் பெண்கள் சிறப்பு மருத்துவ துறையின் கீழ், **"ஒவ்வாத கர்ப்ப கால விளைவுகளை பேறு காலத்தின் மூன்றாவது மாதத்திலேயே (11-13வாரம்+6நாட்கள்) கர்ப்பப்பை தமனி டாப்ளர் ஸ்கேன் மூலம் தெரிந்து கொள்ளுதல்"** என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி: மரு. பாலசுதா D.G.O., D.N.B.,

பேராசிரியர், மகப்பேறு மற்றும் பெண்கள் சிறப்பு மருத்துவத் துறை

ஆய்வு மேற்கொள்வதற்கான அடிப்படை:

கர்ப்பப்பை தமனி டாப்ளர் ஸ்கேன் ஆனது இரண்டாவது மூன்று மாத பேறு காலத்தில் பின்னதாக வரக்கூடிய உயர் இரத்த அழுத்தம் மற்றும் சிசுவின் வளர்ச்சியில் தடை போன்றவற்றை அறிந்து கொள்ள உதவும் கருவியாக பரவலாக ஆய்வு செய்யப்பட்டது. இந்த கருவியை முதல் மூன்று மாத பேறு காலத்திலேயே முன்னதாக வரும் உயர் இரத்த அழுத்தம் மற்றும் ஒவ்வாத கர்ப்ப கால விளைவுகளை கண்டு அறியலாம்.

ஆய்வின் நோக்கம்:

முதல் மூன்று மாத பேறு காலத்தில் செய்யப்படும் கர்ப்பப்பை தமனி டாப்ளர் ஸ்கேன் மற்றும் ஒவ்வாத கர்ப்பகால விளைவுகள் இவற்றுக்கு இடையே உள்ள தொடர்பை ஆராய்தல்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை: 150

ஆய்வில் பங்கு பெறுவோர்மற்றும் வயது: ஒற்றை கருவுற்ற கர்ப்பினிப் பெண்கள்

ஆய்வு மேற்கொள்ளும் இடம்: வெளி நோயாளிகள் பிரிவு, மகப்பேறு மற்றும் பெண்கள் சிறப்பு மருத்துவத்துறை, பூ. சா. கோ மருத்துவ கல்லூரி மருத்துவமனை, கோயமுத்தூர்

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த ஆய்விற்காக சேகரிக்க உள்ளோம்.

ஆய்வு செய்யப்படும் முறை: கர்ப்பப்பை தமனி டாப்ளர் ஸ்கேன் மூலம் கர்ப்பப்பையின் இரத்த ஓட்ட தன்மையை அறிதல்

முதன்மை நேர்காணல்: 10 நிமிடங்கள்

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் **5 வருடங்கள்** பாதுகாக்கப்படும். இந்த தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்தப் படும்/பயன்படுத்தப் பட மாட்டாது.

ஆய்வில் பங்குபெறுவதால் ஏற்படும் பலன்கள்:
- கர்ப்ப காலத்தின் பின்பகுதியில் ஏற்படும் விளைவுகளை முன்னதாகவே கணித்து அதற்கான சிகிச்சை செய்வதின் மூலம் பக்க விளைவுகளை தடுத்தல் அல்லது குறைத்தல்.
- குழந்தை பிறப்பின் நேரத்தை திட்டமிடுதல்.

ஆய்வில் பங்கேற்பதால் ஏற்படக் கூடிய அசௌகரியங்கள் / பக்க விளைவுகள்: இதனால் எந்த அசௌகரியமோ, பக்க விளைவுகளோ ஏற்படாது.

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும்?
ஆய்வின் முடிவுகள், பிற்காலத்தில் ஒவ்வாத கர்ப்ப காலத்தில் ஏற்படும் விளைவுகளை பேறு காலத்தின்போது முதற்பகுதியிலேயே அறிந்து கொள்வதற்கும் அதற்கான அடுத்த கட்ட மருத்துவ சிகிச்சை முன்னதாகவே அளிப்பதற்கும் உதவப்படும்.

இந்த ஆய்வின் கேள்விகளுக்கு பதிலளிப்பதோ, இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுப்பதிலோ உங்களுக்கு ஏதேனும் அசௌகரியங்கள் இருந்தால், எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு. எப்பொழுது வேண்டுமானாலும் ஆய்விலிருந்து விலகும் உரிமை உங்களுக்கு உள்ளது. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சை முறையில் எந்த வித பாதிப்பும் இருக்காது என்று உங்களுக்கு உறுதியளிக்கிறோம். மருத்துவ மனையில் நோயாளிகளுக்கு அளிக்கப்படும் சேவைகளை நீங்கள் தொடர்ந்து பெறலாம். இந்த ஆய்வில் பங்கேற்க ஒப்புக்கொள்ளுவதால் வேறு எந்த விதமான கூடுதலான பலனும் உங்களுக்குக் கிடைக்காது. நீங்கள் அளிக்கும் தகவல்கள் இரகசியமாக வைக்கப்படும். ஆய்வில் பங்கேற்பவர்கள் பற்றியோ அவர்கள் குடும்பத்தைப் பற்றியோ எந்தத் தகவலும் எக்காரணம் கொண்டும் வெளியிடப்படாது என்று உறுதியளிக்கிறோம். நீங்கள் அளிக்கும் தகவல்கள் / இரத்த மாதிரிகள் / திசு மாதிரிகள் அங்கீகரிக்கப்பட்ட ஆய்விற்கு மட்டுமே பயன்படுத்தப்படும். இந்த ஆய்வு நடைபெறும் காலத்தில் குறிப்பிடத்தகுந்த புதிய கண்டுபிடிப்புகள் அல்லது பக்க விளைவுகள் ஏதும் ஏற்பட்டால் உங்களுக்குத் தெரிவிக்கப்படும். இதனால் ஆய்வில் தொடர்ந்து பங்கு பெறுவது பற்றிய உங்கள் நிலைப்பாட்டை நீங்கள் தெரிவிக்க ஏதுவாகும்.

ஆய்வுக்குட்படுபவரின் ஒப்புதல்: இந்த ஆய்வைப் பற்றிய மேற்கூறிய தகவல்களை நான் படித்து அறிந்து கொண்டேன் / ஆய்வாளர் படிக்கக் கேட்டுத் தெரிந்து கொண்டேன். ஆய்வினைப் பற்றி நன்றாகப் புரிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற ஒப்புக்கொள்கிறேன். இந்த ஆய்வில் பங்கேற்பதற்கான எனது ஒப்புதலை கீழே கையொப்பமிட்டு . கை ரேகை பதித்து நான் தெரிவித்துக் கொள்கிறேன்.

பங்கேற்பாளரின் பெயர், முகவரி:

பங்கேற்பாளரின் கையொாப்பம் / கை ரேகை / சட்டப்பூர்வ பிரதிநிதியின் கையொாப்பம்:

தேதி   :

ஆய்வாளரின் கையொாப்பம் :
தேதி   :

ஆய்வாளரின் தொலைபேசி எண்: 9585093324
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அலுவலக் நேரத்திற்குப்பின்: 9865561463

PROFORMA

Name   :

Age   :

S. No.   :

OP No.   :

IP No.   :

Unit   :

Parity Index   :

LMP   :   EDD   :

Gestational Age:

Menstrual H/o:

Obstetric H/o:

Family H/o PIH:

      Mother / Sister

Medical H/o:

      None

      DM

      HTN

      APLA

      Others

Medication during pregnancy:

Parameters will be monitored	I - Trimester	II - Trimester	III - Trimester
GA by LMP			
GA by VSG			
Growth Disparity			
Doppler Study — Ut.A			
Doppler Study — U.A			
Doppler Study — MCA			
BP Monitoring			
Protienuria			
Pre – Eclampsia			
Eclampsia			
Fetal growth restriction			
Ante partum Hemorrhage			
Liquor Volume			
APLA $+^{ve}$			
Abortion (Unexplained)			

Abbreviations: NA – Not Applicable,   N = Normal   Ut.A – Uterine Artery,

UA-Umbilical Artery,   MCA-Middle Cerebral Artery

Pregnancy Outcome   -   Term / Preterm

Type of Delivery   -   Induced / Spontaneous

Mode of Delivery   -   Normal / Caesarean

    If caesarean Section, Indication   -

Intrapartum Complications   -   Yes / No

If yes,

Baby Details:

    Sex   :

    Weight   :

    APGAR   :

    NICU Admission:

ABBREVIATIONS

S.NO   -   Serial Number

OP NO   -   Outpatient Number

PRE.O.H   -   Previous Obstetric History

FAM H/O   -   Family History

O.MED.H   -   Other Medical History

APLA   -   Antiphospholipid Antibody

G.AGE AT D -   Gestational Age at Delivery

MOD   -   Mode of Delivery

G.HTN   -   Gestational Hypertension

C.HTN   -   Chronic Hpertension

PE   -   Pre ecalmpsia

IUGR   -   Intra Uterine Growth Restriction

OLIGO   -   Oligohydramnios

GDM   -   Gestational Diabetes Mellitus

GDM D   -   GDM on Diet

GDM OHA   -   GDM on Oral Hypoglycemic Index

BOH	-	Bad Obstetric History
IUD	-	Intra Uterine Death
NND	-	Neonatal Death
RHD	-	Rheumatic Heart Disease
TM	-	Term

F – Father ; M – Mother

N – Not Started ; Y – Started

LT DN +	-	Left Uterine Diastolic Notch present
RT DN +	-	Right Uterine Diastolic Notch present
B/L UA N+	-	Bilateral Uterine Artery Notch+
ABS D FL	-	Absent Diastolic Flow
Ano fts	-	Anomalous Fetus
NVD	-	Normal Vaginal Delivery
VAVD	-	Vaccum Assisted Vaginal Delivery
EM/EL LSCS	-	Emergency / Elective Caesarean Section
APLA	-	Anti Phospholipid Antibody Syndrome

MASTER CHART

S.NO	OP NUM	AGE(yrs)	AGE(yrs)	PARITY	PRE .O.H	FAM H/O	G.AGE	U/A (L)	U/A (R)	AVR U/A	ASPIRIN	2 - DOPP	3 - DOPP	IUGR	OLIGO	G.HTN	PRE - ECL	ECLAM	HELLP	APLA	O.MED.H	GAGE@D	MOD	B.WT
1	10/11495	22	22	P	Nil	Nil	12w+4d	0.9	0.48	0.69	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	3.01
1	15/74037	20	20	G2A1	Nil	Nil	12w+4d	1.1	1.2	1.15	N	NL	QUIT	-	-	-	-	-	-	-	-	-	-	-
1	15/84632	29	29	P	Nil	Nil	12W+3d	1.47	1.56	1.5	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	VAVD	3.2
1	12/85241	23	23	G3P1L1A1	CS	Nil	12W+2d	2	1.8	1.9	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EM - LSCS	2.72
1	15/83371	20	20	P	Nil	Nil	11W+5d	1.98	1.63	1.8	N	NL	NL	A	A	A	A	A	A	ND	A	37W+	NVD	2.77
1	15/67194	29	29	G2P1L1	Nil	Nil	12W+2d	1.26	1.47	1.36	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	VAVD	3.3
1	14/49505	23	23	P	Nil	Nil	12W+3d	0.85	2.26	1.55	N	NL	NL	A	A	A	A	A	A	ND	A	40W	NVD	3.32
1	15/84451	20	20	P	Nil	Nil	12W+5d	2.28	1.2	1.74	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.48
1	13/21106	30	30	G2P1L1	G.THN,CS	F-HTN	12W+5d	1.73	2.15	1.94	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EL - LSCS	3.91
1	15/85453	21	21	P	Nil	Nil	12w+4d	1.83	1.8	1.81	N	NL	NL	P	A	P	A	A	A	ND	Hypo	38w+	NVD	2.69
1	15/84561	25	25	P	Nil	Nil	12W+6d	1.52	2	1.76	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	VAVD	2.95
1	16/00716	27	27	G2P1L1	Nil	Nil	12W+3d	0.58	0.69	0.635	N	NL	NL	A	A	A	A	A	A	ND	EMPTY SS	38W+	EM - LSCS	2.03(SGA)
1	16/03603	27	27	G2A1	Nil	Nil	13W+5d	1.56	1.8	1.68	N	NL	NL	A	A	A	A	A	A	ND	A	40W	EM - LSCS	3.19
1	12/17947	26	26	G4P2L1A1	NND,CS	F&M HTN	12W+2d	1.18	1.54	1.36	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EM - LSCS	2.75
1	15/80483	27	27	G2A1	Nil	Nil	11W+5d	0.76	1.03	0.89	N	NL	NL	A	A	A	A	A	A	A	A	QUIT	-	-
1	15/86401	34	34	G2P1L1	Nil	Nil	12W+5d	1.96	1.9	1.9	N	NL	NL	A	P	A	A	A	A	A	GDM - D	40W	EM - LSCS	3.7
1	14/19430	31	31	G2P1L1	Nil	Nil	13W+5d	1.72	0.84	1.28	N	NL	NL	A	A	A	A	A	A	A	A	40W	NVD	3.29
1	15/83248	22	22	P	Nil	Nil	12w+4d	1.53	1.11	1.32	N	NL	NL	A	A	A	A	A	A	A	A	39W+	NVD	3.11
1	15/49755	28	28	G1A1	Nil	Nil	12wks	1.2	1	1.1	N	QUIT	-	-	-	-	-	-	-	-	-	-	-	-
1	15/85169	24	24	P	Nil	Nil	13w+4d	2.13	1.57	1.85	N	NL	NL	A	A	A	A	A	A	A	GDM - D	40W	EM - LSCS	3.3
1	15/65397	21	21	G2A1	Nil	Nil	12wks	2.17	1.87	2.02	N	NL	NL	A	A	A	A	A	A	A	A	40W	VAVD	3.1
1	12/77298	26	26	P	Nil	Nil	12w+5d	1.09	1.15	1.12	N	NL	NL	A	A	A	A	A	A	A	A	39W+	VAVD	3.12
1	13/19418	27	27	G1P1L1	Nil	M&F HTN	11w+4d	2.06	1.54	1.8	N	NL	NL	A	A	A	A	A	A	A	A	40w	VAVD	2.97
1	16/01405	23	23	P	Nil	Nil	13wks	1.6	1.3	1.45	N	NL	NL	A	A	A	A	A	A	ND	A	40W	NVD	2.83
1	15/86985	20	20	G3A2	Nil	Nil	11w+5d	1.19	1.28	1.23	N	NL	QUIT	-	-	-	-	-	-	-	-	-	-	-
1	15/29237	29	29	P	Nil	Nil	12W+2d	1.2	1	1.1	N	NL	NL	A	A	A	A	A	A	ND	A	40W	VAVD	3.2
1	15/86325	25	25	P	Nil	Nil	11w+6d	2	1.6	1.8	N	NL	NL	A	A	A	A	A	A	ND	A	40W	NVD	3.27
1	15/87244	24	24	P	Nil	Nil	12W+5d	1.4	1.2	1.3	N	NL	NL	A	A	A	A	A	A	ND	GDM - D	40w	NVD	3.78
1	15/87376	23	23	P	Nil	Nil	12w+4d	1.5	2	1.75	Y	B/L UA N+	NL	A	A	A	A	A	A	ND	A	37W+	NVD	2.5
1	16/05954	25	25	P	Nil	Nil	12w+5d	1.4	2.18	1.79	N	NL	NL	A	A	A	A	A	A	ND	A	40W	EM - LSCS	3.36
1	16/02294	26	26	G2P1L1	CS	Nil	11W+5d	1.8	2	1.9	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EL - LSCS	3.05
1	15/80703	30	30	G2P2L2	CS	F - HTN	12W+4d	1.6	2	1.8	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EL - LSCS	3.11
1	15/84607	20	20	P	Nil	Nil	12W+2d	2	1.73	1.86	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.75
1	15/87962	23	23	P	Nil	Nil	12W+1d	1.4	2	1.7	N	NL	NL	A	A	A	A	A	A	ND	Hypo	38W+	NVD	2.94
1	15/85640	30	30	P	Nil	Nil	13WKS	1.03	1	1	N	QUIT	-	-	-	-	-	-	-	-	-	-	-	-
1	14/08870	20	20	G2P1L1	Nil	Nil	12W+2d	0.98	0.59	0.78	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	EM - LSCS	3.59
1	16/30572	23	23	P	Nil	Nil	12W+2d	1.1	1.5	1.3	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.67
1	16/38101	26	26	P	Nil	Nil	12WKS	1.62	1.65	1.63	N	NL	NL	A	A	A	A	A	A	ND	GDM - DS	38W+	EM - LSCS	3.88
1	16/38374	25	25	P	Nil	Nil	12W+5d	1	1.7	1.35	N	NL	NL	A	A	A	A	A	A	ND	A	37W+	EM - LSCS	2.92
1	16/37165	25	25	P	Nil	Nil	12wks	0.8	1.5	1.15	N	NL	NL	A	A	A	A	A	A	ND	A	QUIT	-	-
1	16/36389	25	25	P	Nil	Nil	12W+1d	1.66	1.7	1.68	N	NL	NL	P	A	A	A	A	A	ND	A	39W+	NVD	2.52
1	16/37369	26	26	P	Nil	Nil	12W+1d	1.1	0.75	0.92	N	NL	NL	A	P	A	A	A	A	ND	A	35W+	NVD	2.46
1	14/26201	25	25	G1A1	Molar pg	Nil	12W+6d	1	1.2	1.1	N	NL	NL	A	A	A	A	A	A	ND	A	40W	VAVD	2.68
1	13/73650	27	27	P	Nil	Nil	12w+4d	1.1	0.9	1	N	NL	NL	A	P	A	A	A	A	ND	A	38W+	NVD	2.9
1	16/38342	23	23	P	Nil	Nil	12WKS	1.2	1.1	1.15	N	NL	-	-	-	-	-	-	-	-	-	-	-	-
1	15/74745	23	23	G2A1	Nil	Nil	12W+6d	1.18	1.76	1.47	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.68
1	14/33264	34	34	G4P2L1A1	BOH,RHD	F&M HTN	13W+1d	1.28	1.29	1.28	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	3.04
1	12/52151	22	22	G3P1L1A1	Nil	Nil	12W+5d	1.63	2.09	1.845	N	NL	NL	P	A	A	A	A	A	ND	A	38W+	NVD	2.6
1	15/43926	25	25	P	Nil	Nil	12w+4d	2	1.4	1.7	N	NL	NL	A	A	A	A	A	A	ND	GDM - D	40W	FAVD	3.63
1	11/59065	22	22	G2P1L1	Nil	Nil	13Wks	1.25	1.1	1.175	N	NL	NL	A	A	A	A	A	A	ND	A	40W	NVD	3.67
1	16/02978	33	33	G2P1L1	Nil	Nil	12W+1d	1.57	1	1.28	N	NL	NL	A	A	A	A	A	A	ND	A			
1	16/05770	24	24	G2P1L1	CS	Nil	12W+6d	2	1.33	1.66	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EM - LSCS	2.87
1	15/22670	20	20	G2P1L1	Nil	Nil	12W+6d	1.9	1.5	1.7	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	NVD	2.94
1	16/12495	22	22	G2P1L1	Nil	Nil	13Wks	1.3	1.9	1.6	N	-	-	-	-	-	-	-	-	-	-	-	-	-
1	11/23889	26	26	G3P1L1A1	LSCS	Nil	12W+6d	1.4	1.4	1.4	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	EL - LSCS	3.11
1	16/12550	25	25	P	Nil	Nil	12W+1d	1.2	1.6	1.4	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	VAVD	3.32
1	16/12680	19	19	P	Nil	Nil	12W+5d	0.62	1.84	1.23	N	NL	NL	A	A	A	A	A	A	ND	A	36W+	NVD	2.54
1	14/79019	26	26	G2P1L1	Nil	Nil	12W+2d	1.14	1.19	1.165	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	EM - LSCS	3.05
1	14/26853	20	20	G2P1L1	Nil	Nil	12W+3d	1.4	0.9	1.15	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	NVD	3.23
1	16/20523	29	29	P	Nil	Nil	13wks	1.3	1.59	1.44	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.76
1	10/01517	27	27	G2A1	Nil	Nil	12W+6d	1.41	0.8	1.1	N	NL	NL	A	P	A	A	A	A	ND	DM	38W+	EM - LSCS	2.82
1	13/10943	31	31	G3P1L1A1	Nil	Nil	12W+3d	0.68	1.7	1.19	N	NL	ABS D FL	P	A	A	A	A	A	ND	A	37W+	NVD	2.52
1	15/77283	23	23	P	Nil	Nil	12W+3d	1.5	1.9	1.7	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EM - LSCS	3.13
1	07/83662	29	29	P	Nil	Nil	12w+4d	1.06	1.4	1.23	N	NL	Ano fts	-	-	-	-	-	-	-	-	-	-	-
1	11/94144	27	27	G2P1L1	Nil	Nil	12wks	0.98	1.68	1.33	N	NL	NL	A	A	A	A	A	A	ND	GDM - DS	39W+	VAVD	3.65
1	15/77788	27	27	P	Nil	Nil	12W+5d	1.89	2	1.94	N	NL	NL	A	A	A	A	A	A	ND	GDM - D	36W+	NVD	2.3,SGA
1	16/22515	25	25	P	Nil	Nil	11W+4d	1.71	0.96	1.33	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	NVD	3.2
1	16/18821	23	23	P	Nil	Nil	12wks	1.8	1.4	1.6	N	NL	NL	A	A	A	A	A	A	ND	A	40W	EM - LSCS	3.87
1	07/63985	29	29	P	Nil	Nil	12W+5d	1.56	1.16	1.36	N	NL	NL	A	P	A	A	A	A	ND	A	37W+	NVD	2.58
1	16/10899	24	24	P	Nil	Nil	12W+2d	1.63	1.84	1.73	N	NL	NL	A	A	A	A	A	A	ND	A	40W	EM - LSCS	3.87
1	13/39535	26	26	G2P1L1	Nil	Nil	12W+6d	0.69	1.93	1.31	N	NL	NL	A	A	A	A	A	A	ND	A	39W+	NVD	3.48
1	13/52758	27	27	G3P1L1A1	Nil	Nil	12W+2d	1.1	1.2	1.15	N	NL	NL	A	A	A	A	A	A	ND	GDM - D	40W	NVD	3.77
1	16/15264	28	28	G2A1	Nil	Nil	11w+6d	1	1	1	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.93
1	16/25881	22	22	G3P1L1A1	Nil	Nil	12w+4d	1.4	1.3	1.35	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	NVD	2.68
1	16/20782	27	27	G3P1L1A1	CS	Nil	12w+6d	1.1	1.2	1.15	N	NL	NL	A	A	A	A	A	A	ND	A	38W+	EL - LSCS	3.08
2	16/18294	25	25	P	Nil	Nil	11w+5d	3.6	4.6	4.1	Y	NL	NL	A	A	A	A	A	A	ND	A	35W	NVD	2.15
2	11/39261	27	27	G5P1L1A3	Nil	Nil	14w+6d	2.8	1.8	2.3	Y	NL	NL	A	P	A	A	A	A	ND	C.THN	34W+	NVD	2.11
2	14/08459	25	25	P	Nil	Nil	12w+4d	1.8	2.9	2.35	N	NL	NL	A	A	A	A	A	A	ND	S.VSD	36W	NVD	2.37
2	16/09140	25	25	G2P2L2	CS	Nil	11w+3d	2.27	2.8	2.5	N	NL	ABS D FL	A	A	A	A	A	A	ND	A	QUIT	-	-
2	16/15384	24	24	P	Nil	Nil	12w+4d	2.4	2.2	2.3	N	NL	Nl	A	A	A	A	A	A	ND	A	39W+	NVD	3.03
2	16/18000	25	25	P	Nil	Nil	13 wks	1.7	2.3	2	N	NL	Nl	A	A	A	A	A	A	ND	A	38W	NVD	2.48
2	16/10874	27	27	P	Nil	Nil	12w+2d	2.49	1.29	1.89	N	NL	Nl	A	A	A	A	P	A	ND	A	38W	EM.LSCS	3.09
2	16/16356	22	22	P	Nil	Nil	12w+2d	2.52	2.25	2.38	N	NL	Nl	A	A	A	P	A	A	ND	ASTHMA	38W+	VAVD	3.26
2	12/57441	26	26	G3P1L1A1	Nil	F-HTN	13W+1d	2.5	1.1	1.8	N	NL	Nl	A	A	A	A	A	A	ND	Hypo	QUIT	-	-
2	16/18988	33	33	G2P1L1	Nil	M-HTN	12W+3d	1.1	2.5	1.8	Y-Age	NL	Nl	A	A	A	A	A	A	ND	GDM - D	38W	NVD	3.12
2	14/62612	26	26	G2P1L1	Nil	Nil	12w+3d	2.4	1.56	1.98	N	NL	Nl	A	A	A	A	A	A	ND	A	38W	NVD	3.53
2	16/17404	35	35	G2P2L2	CS	F&M-HTN	12W+1d	1.2	2.7	1.95	N	QUIT	Nl	A	A	A	A	A	A	ND	GDM-OHA	38W	ELE-LSCS	2.87
2	16/16998	26	26	P	Nil	Nil	11w+6d	3.1	1.57	2.3	N	QUIT	-	-	-	-	-	-	-	-	-	-	-	-
2	16/19482	23	23	P	Nil	Nil	12w+5d	1.97	2.3	2.13	N	LT - D N +	NL	A	A	A	A	A	A	ND	A	39W+	EM.LSSCS	3.25
2	16/19883	39	39	G2P1L1	CS	M-DM	11W+4d	3.9	1.89	2.85	N	NL	QUIT	-	-	-	-	-	-	-	-	-	-	-
2	16/12542	31	31	P	Nil	Nil	11w+4d	2.3	2	2.15	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W+	EM.LSSCS	2.94
2	16/13606	24	24	P	Nil	Nil	12W+5d	2.3	1	1.65	y	Nl	Nl	A	A	A	A	A	A	ND	A	38W+	NVD	2.62
2	16/19190	20	20	G1P2L0	2NND	Nil	12w+2d	2.4	1.5	1.95	N	Nl	Nl	A	A	A	A	A	A	A	GM -OHA	QUIT	-	-
2	16/21393	24	24	G1P1L1	Nil	Nil	12w+5d	2.8	2.3	2.55	y	QUIT	-	-	-	-	-	-	-	-	-	-	-	-
2	16/09994	28	28	G2A1	Nil	Nil	12w+2d	2.3	0.78	1.54	N	Nl	Nl	A	A	A	A	A	A	ND	A	38w+	EM.LSSCS	3.75
2	16/33061	27	27	G2P1L1	Nil	Nil	12+2d	2.3	2	2.15	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	EL-LSCS	2.25(SGA)
2	16/36902	23	23	P	Nil	Nil	11w+4d	1.2	3	2.1	N	Nl	Nl	A	A	A	A	A	A	ND	A	36w	NVD	2.61
2	16/34446	24	24	P	Nil	Nil	12W+2d	2.45	1.95	2.2	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	NVD	2.23(SGA)
2	12/56875	26	26	G2P1L1	Nil	Nil	11w+5d	2.07	2.3	2.18	N	Nl	Nl	A	A	A	A	A	A	ND	GDM - D	39W	NVD	3.03
2	16/372000	25	25	P	Nil	Nil	12w+2d	2.09	3.37	2.73	y	Nl	Nl	A	A	A	A	A	A	ND	A	39W	VAVD	2.71
2	16/36312	25	25	P	Nil	Nil	12W+5d	1.8	3.1	2.45	N	Nl	NL	A	A	A	A	A	A	ND	GDM-OHA	40W	EM-LSCS	3.45
2	16/36490	29	29	G2P1L1	Nil	M-HTN	12W+2d	2.5	1.08	1.79	N	Nl	Nl	A	A	A	A	A	A	ND	Hypo	40W	NVD	3.36
2	15/87542	30	30	G2A1	Nil	F-HTN&DM	12W+3d	2.29	2.76	2.5	Y	RT-DN+	QUIT	-	-	-	-	-	-	-	-	-	-	-
2	16/46761	31	31	P	Nil	Nil	12w+2d	1.4	2.3	1.85	N	Nl	Nl	A	A	A	A	A	A	ND	A	39w	NVD	3.1
2	16/34726	24	24	P	Nil	M-DM	13W+2d	2.3	1.4	1.85	y	Nl	Nl	A	A	A	A	A	A	ND	A	39W	NVD	3.37
2	16/34982	26	26	P	Nil	Nil	12w+2d	1.96	2.98	2.45	N	Nl	Nl	A	A	A	P	A	A	ND	A	36W+	NVD	2.62
2	16/34636	25	25	P	Nil	Nil	12W+5d	2.7	2.8	2.75	Y	LT - D N +	NL	A	A	A	A	A	A	ND	A	35W+	NVD	1.77(SGA)
2	16/38467	27	27	G3P1L1A1	PE	M-HTN	13W+4d	2.4	1.7	2.05	N	Nl	Nl	A	A	A	A	A	A	ND	A	QUIT	-	-
2	13/88604	24	24	G3P1L1A1	Nil	Nil	12W+1d	3.58	1.71	2.64	y	Nl	Nl	A	A	A	A	A	A	ND	A	37W+	NVD	2.86
2	08/92696	31	31	G4P1L1A2	Nil	F-HTN	13w+3d	2.26	2.37	2.3	N	Nl	Nl	A	A	A	A	A	A	ND	A	34W	EM - LSCS	1.57
2	10/01300	32	32	G2P1L1	Nil	Nil	12w+3d	2.89	1.82	2.35	N	Nl	Nl	A	A	A	A	A	A	ND	GDM-OHA	38W+	NVD	2.78
2	12/31356	27	27	G4P2L1A2	TM - IUD	Nil	12w+2d	2.3	2.1	2.2	Y	Nl	Nl	A	A	A	A	A	A	ND	A	38w+	NVD	3.25
2	16/49812	31	31	P	Nil	Nil	12+6d	1.56	3.14	2.35	N	Nl	Nl	P	A	P	A	A	A	ND	A	38W	EM -LSCS	2.5
2	16/53431	20	20	P	Nil	Nil	12W+2d	2.3	2	2.2	N	Nl	QUIT	-	-	-	-	-	-	-	-	-	-	-
2	14/53550	26	26	P	Nil	Nil	13wks	1.2	2.4	1.3	N	Nl	Nl	P	A	A	A	A	A	ND	A	39W	VAVD	3.07
2	16/39147	26	26	P	Nil	Nil	11w+6d	2.05	2.3	2.17	N	Nl	Nl	A	A	A	A	A	A	ND	A	35W	EM -LSCS	1.34
2	16/80652	25	25	P	Nil	Nil	12wks	1.79	2.71	2.25	N	Nl	Nl	A	A	A	P	A	A	ND	A	38W	NVD	2.85
2	16/41083	28	28	P	Nil	M-HTN	12W+1d	2.03	3.01	2.52	Y	Nl	Nl	A	A	A	P	A	A	ND	A	39W	NVD	3.01
2	16/59972	25	25	G3P1L1A1	Nil	Nil	12W+6d	2.3	2	2.15	N	Nl	Nl	A	A	A	A	A	A	ND	GDM - D			
2	13/23037	29	29	G2P1L1	CS	Nil	12w+3d	2.6	1.4	2	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	EM - LSCS	2.35
2	16/38284	25	25	P	Nil	Nil	12w+3d	2.4	1.58	1.99	N	RT-DN+	Nl	A	A	A	A	A	A	ND	A	36W	NVD	2.8
2	16/35382	19	19	P	Nil	Nil	12w+4d	1.6	2.3	1.95	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	NVD	2.69
2	16/36312	25	25	P	Nil	Nil	12w+5d	1.8	3.1	2.45	N	Nl	Nl	A	A	A	A	A	A	ND	GDM - OHA	38W	EM - LSCS	3.45
2	16/45237	25	25	P	Nil	Nil	12WKS	2.27	2.66	2.46	N	Nl	Nl	A	A	A	A	A	A	ND	GDM - D	39W	VAVD	2.37(SGA)
2	16/34474	19	19	P	Nil	Nil	12w+5d	0.5	2.5	1.5	N	Nl	Nl	A	A	A	A	A	A	ND	Hypo	38W	NVD	2.37(SGA)
2	16/57056	26	26	P	Nil	Nil	12w+3d	2.76	0.91	1.83	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	NVD	2.79
2	16/16319	26	26	P	Nil	Nil	11w+5d	1.8	2.7	2.25	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	VAVD	3.02
2	16/46761	18	18	P	Nil	Nil	12w+2d	1.4	2.3	1.85	N	QUIT	-	-	-	-	-	-	-	-	-	-	-	-
2	16/44876	24	24	G3P1L1A1	CS	Nil	12w+4d	2	2.8	2.4	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	EL - LSCS	3.02
2	16/44327	22	22	P	Nil	Nil	12w+4d	1.4	2.8	2.1	N	Nl	Nl	A	A	A	A	A	A	ND	A	39W	NVD	3.19
2	12/79895	27	27	G2P1L1	Nil	M- HTN	13WKS	2.6	4.1	3.35	Y	Nl	Nl	A	A	A	A	A	A	ND	A	38W	EM - LSCS	2.12
2	16/57529	25	25	G2P1L1	CS	Nil	13W+4d	2.58	3.11	2.86	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	EL - LSCS	2.73
2	16/20483	32	32	G6P2L0A3	2NND	Nil	12w+4d	2.6	1.54	2.07	Y+HEPAR	Nl	Nl	A	A	A	A	A	A	DONE - P	P	38W	EL - LSCS	2.45(SGA)
2	16/39917	29	29	P	Nil	Nil	12WKS	2.3	1.91	2.1	N	Nl	Nl	A	A	A	A	A	A	ND	A	40W	NVD	3.21
2	07/38975	24	24	G2P1L1	Nil	Nil	12W+4d	1.1	4	2.58	N	Nl	Nl	A	A	A	A	A	A	ND	A	40W	NVD	3.5
2	16/39651	37	37	P	Nil	F&M-HTN	13WKS	2.69	1.8	2.26	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	VAVD	2.27
2	16/34636	23	23	P	Nil	M-HTN	12w+5d	2.7	2.8	2.75	Y	RT-DN+	Nl	A	A	A	A	A	A	PE	A	34W	NVD	1.77
2	12/83000	32	32	G2P1L1	CS	F-HTN	12W+1d	1.64	2.45	2.03	N	Nl	Nl	A	A	A	A	A	A	ND	A	37W	EL - LSCS	3.07
2	16/46325	24	24	P	Nil	Nil	13WKS	1.3	2.3	1.3	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	NVD	2.9
2	11/55357	26	26	G3P2L2	Nil	Nil	13W+1d	2.29	2.4	2.34	N	Nl	Nl	A	A	A	A	A	A	ND	A	QUIT	-	-
2	16/51363	27	27	P	Nil	Nil	12WKS	2.8	2.7	2.75	N	Nl	Nl	P	A	P	A	A	A	ND	A	38W	NVD	2.4
2	13/46571	23	23	G2P1L1	Nil	Nil	12w+3d	2.3	2.3	2.22	N	Nl	Ano fts	-	-	-	-	-	-	-	-	-	-	-
2	16/84981	27	27	P	Nil	Nil	12w+2d	3.71	2.27	2.99	Y	Nl	Nl	A	A	A	A	A	A	ND	A	33W	VAVD	2.39
2	16/34638	21	21	P	Nil	Nil	12w+2d	2.8	2.8	2.8	Y	LT - D N +	Nl	A	A	A	A	A	A	PE	A	33W	NVD	1.7
2	11/75233	22	22	G3P1L1A1	Nil	Nil	12w+5d	4	2.8	3.45	Y	Nl	Nl	A	A	A	A	A	A	ND	A	40W	NVD	3.19
2	15/89132	24	24	P	Nil	Nil	12w+4d	2.6	2.2	2.4	Y	Nl	Nl	A	A	A	A	A	A	ND	PE	36W	EM - LSCS	2.91
2	15/87279	28	28	P	Nil	Nil	12w+6d	2.9	2.2	2.55	N	Nl	Nl	A	A	A	A	A	A	ND	A	38W	NVD	2.25
2	15/88236	21	21	G2P1L0	IUD	Nil	12w+4d	2.3	1.4	1.85	N	Nl	Nl	P	A	A	A	A	A	ND	A	36W	NVD	2.3
2	16/06497	29	29	P	Nil	Nil	13W+1d	2.64	1.8	2.22	N	Nl	Nl	A	A	A	A	P	A	ND	PE	38W	EM - LSCS	2.93
2	15/73097	29	29	G2A1	Nil	Nil	13WKS	1.8	2.5	2.15	Y	LT - D N +	Nl	P	A	A	A	A	A	ND	A	38W	VAVD	2.3