
**“EVALUATION OF UTERINE ARTERY DOPPLER AT 11-
13⁺⁶ WEEKS FOR PREDICTION OF PRE-ECLAMPSIA-A
DESCRIPTIVE OBSERVATIONAL STUDY”**

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**KLE UNIVERSITY, BELAGAVI,
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ABSTRACT

Background and objectives

Various measurement techniques and impedance indices have been used to evaluate the relationship between uterine artery Doppler velocimetry and adverse pregnancy outcomes. This study was aimed to evaluate bilateral uterine artery Doppler in pregnant women with gestational age between 11+0 to 13+6 weeks in the prediction of preeclampsia and IUGR.

Methodology

The present one year longitudinal prospective cohort study conducted on 117 pregnant women with gestational age between 11+0 to 13+6 weeks attending antenatal checkup in the Department of Obstetrics and Gynecology, KLES Dr Prabhakar Kore Charitable Hospital and Medical Research Center, Belagavi from January 2016 to December 2016.

Results

The most common age group was between 21 to 25 years (50.43%) and the mean age was 24.41 ± 4 years. Most of the women were gravida 2 (44.44%). The pulsatility index ranged between 2% to 99%. Majority of the women (89.74%) had normal pulsatility index (<95%) and high (≥95) in 10.26% of the women. Most of the women (57.26%) had vaginal delivery and 42.74% underwent for LSCS. In this study out of 117 women, 30 (25.64%) women had comorbidities. Most common comorbidity was FGR (13.68%) followed by preeclampsia (7.69%). There were five preterm deliveries. Significantly higher number of women with pulsatility index ≥95% had preeclampsia (55.56%) ($p < 0.001$) and the sensitivity of PI in prediction of preeclampsia was 55.56% with specificity of 93.52% and there was moderate

agreement with Kappa value of 0.426 (95% CI 0.146 to 0.705). No association was found between pulsatility index and FGR ($p=0.228$). The present study showed positive association between PI of $\geq 95\%$ with development FGR in pregnancy complicated by preeclampsia ($p=0.008$).

Conclusion and interpretation

Based on the findings of this study it may be concluded that, PI of $\geq 95\%$ is strongly associated with development of preeclampsia and FGR in pregnancy complicated by preeclampsia.

Key words

Fetal growth restriction; Preeclampsia; Uterine artery Doppler waveform;

ABBREVIATIONS

ACOG	-	American College of Obstetricians and Gynaecologists
NIH	-	National Institutes of Health
RCOG	-	Royal college of Obstetricians and Gynaecologists
LSCS	-	Lower segment caesarean section.
VBAC	-	Vaginal birth after caesarean.
TOLAC	-	Trial of labour after caesarean.
ERCS	-	Elective repeat caesarean section
SD	-	Standard deviation.
EFW	-	Expected Fetal Weight
ST	-	Scar Tenderness
CTG	-	Cadiotochograph
NPL	-	Non Progress of Labour
CPD	-	Cephalopelvic disproportion
TMSL	-	Thick Meconium Stained Liquor
FT	-	Fetal Tachycardia
FD	-	Fetal distress
SD	-	Scar Dehiscence
CS	-	Cesarean Section

PROM	-	Premature rupture of membrane.
FM	-	Fetal Macrosomia
BMI	-	Body Mass Index
RMT	-	Residual myometrial thickness
AUC	-	Area under the curve
LMP	-	Last menstrual cycle
EDD	-	Expected date of delivery
APH	-	Antepartum haemorrhage
FGR	-	Fetal growth restriction

TABLE OF CONTENTS

SL NO	SECTIONS	PAGE NO.
1	INTRODUCTION	1-3
2	OBJECTIVES	4
3	REVIEW OF LITERATURE	5-32
4	METHODOLOGY	33-38
5	RESULTS	39-53
6	DISCUSSION	54-58
7	CONCLUSION	59
8	SUMMARY	60-62
9	BIBLIOGRAPHY	63-75
10	ANNEXURES	
	ANNEXURE I - INFORMED CONSENT	76-79
	ANNEXURE II –PROFORMA	80-82
	ANNEXURE III–PHOTOGRAPHY	83
	ANNEXURE 3 – ETHICAL CLEARANCE	84
	ANNEXURE IV–KEY TO MASTERCHART	85

LIST OF TABLES

Sl.No.	Particulars	
1	Distribution of women according to the maternal age	40
2	Distribution of women according to the gravida	41
3	Distribution of women according to the body mass index	42
4	Distribution of women according to the Pulsatility index	43
5	Distribution of neonates according to the birth weight	44
6	Distribution of women according to the gestational age at delivery	45
7	Frequency of comorbidities	46
8	Distribution of women according to the comorbidities	47
9	Maternal, clinical and ultrasound characteristics of the study population	48
10	Association of preeclampsia with pulsatility index	49
11	Association of FGR with pulsatility index	50
12	Association of combined FGR and PE with pulsatility index	51
13	Distribution of women according to the gestational age at screening	52
14	Distribution of women according to the gestational age at which preeclampsia was detected	53

LIST OF GRAPHS

Sl.No.	Particulars	Page No.
1	Distribution of women according to the maternal age	40
2	Distribution of women according to the gravida	41
3	Distribution of women according to BMI	42
4	Distribution of women according to the Pulsatility index	43
5	Distribution of neonates according to the birth weight	44
6	Distribution of women according to the gestational age at delivery	45
7	Frequency of comorbidities	46
8	Distribution of women according to the comorbidities	47
9	Association of Pre-eclampsia with pulsatility index	49
10	Association of FGR with pulsatility index	50
11	Association of combined FGR and PE with pulsatility index	51
12	Distribution of women according to the gestational age at screening	52
13	Distribution of women according to the gestational age at preeclampsia	53

LIST OF FIGURES

Sl. No.	Figures	Page no.
1	Flow velocity waveform (FVW) of uterine artery in a non pregnant patient: Characteristics shape of this waveform shows a steep systolic slope, an early diastolic notch and a small amount of diastolic flow.	20
2	FVW in established pregnancy at 20 weeks: Placentation typically results in a low resistance FVW, the disappearance of the notch and an abundance of diastolic flow	20
3	FVW in pregnancy at 12 weeks: Normal Doppler	21
4	FVW in pregnancy at 12 weeks: Increased Resistance on Uterine Artery Doppler	21
5	Flow velocity waveform of the uterine artery with mode, mean, minimum (min) and maximum (max) velocity (V)	23
6	Flow velocity waveform with S (maximum peak systolic frequency D (end-diastolic velocity) and A (mean Doppler shift frequency)	24

INTRODUCTION

Screening test is an intervention designed to identify a disease early so as to enable earlier intervention and treatment so as to reduce mortality and morbidity from the disease.¹

Hypertensive disorders of pregnancy include Gestational hypertension, Preeclampsia and Eclampsia. It forms a triad along with infection and hemorrhage which contributes to maternal morbidity and mortality.²

Globally hypertensive disorders of pregnancy complicate 6-10% of pregnancies. In Africa and Asia, it affects 9% of pregnancies. In India it affects 10-12% of pregnancies and contributes greatly to maternal morbidity and mortality.³

Fetal growth restriction is seen to occur in 3-10% infants which significantly increases the risk of perinatal mortality and morbidity.³

Pre-eclampsia and fetal growth restriction remains important causes of maternal and neonatal complications and death.⁴ Pre-eclampsia contributes to 6% of perinatal deaths and FGR contributes to 10% of perinatal deaths.⁵

Current antenatal care provision is focused on a risk-based approach to monitor for adverse pregnancy outcomes such as preeclampsia, fetal growth restriction, placental abruption, and stillbirth.⁵

In normal pregnancy, there is trophoblastic invasion of spiral arteries which is incorporated into vessel wall and replaces the endothelium, muscular layer and neural tissue. These physiological changes convert spiral arteries from narrow muscular vessels to wide non-muscular channels independent of maternal vasomotor

control. In pre-eclampsia there is impaired trophoblastic invasion and failure of reduction in vascular resistance in uteroplacental circulation. Indirect evidence of impaired placental perfusion in pregnancies destined to develop pre-eclampsia has been provided by uterine artery Doppler which showed increased pulsatility index during both first and second trimester of pregnancy.⁶

The uteroplacental circulation can be assessed by means of Doppler ultrasonography of the uterine arteries. This has been demonstrated to be a reliable , non-invasive procedure. This procedure has been reported in numerous studies to be a promising technique for predicting the level of risk for pre-eclampsia and intrauterine growth restriction. In a normal pregnancy, impeded flow in the uterine artery decreases with increasing gestational age. In a high proportion of pregnancies destined to develop pre-eclampsia, there is co-relation between Doppler study and development of pre-eclampsia.⁴

Uterine artery Doppler ultrasonography may be performed via the transvaginal or transabdominal route in the first or second trimester. The uterine artery is identified with the use of colour Doppler ultrasonography. Pulsed-wave Doppler ultrasonography is then used to obtain waveforms. Various indices can be calculated and assessed.⁴

Studies in which placental bed biopsies were performed on the third quarter of gestation, have reported inappropriate or abnormal trophoblastic invasion as predominant lesion in women with preeclampsia; the mechanism responsible for this failure still remains to be known.⁷ These histologic findings have a good correlation with the increase of resistance to the flow in the uterine arteries evaluated by Doppler⁸

and a relation of this increase in resistance and the subsequent onset of preeclampsia.^{9,10}

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 onset of preeclampsia, intrauterine growth restriction (IUGR), premature placental separation (PPS) and preterm delivery (PTD).¹¹

Earlier uterine Doppler was done in second trimester (22 – 24 weeks), but now for early intervention and management, it is done in first trimester (11-13⁺⁶ weeks) itself.¹¹

Early identification of high risk group for development of PE is also important to determine the potential role of pharmacological interventions starting from first trimester to improve placentation and reduce prevalence of disease and associated complications.⁶

Two of the most challenging areas in antenatal care are prematurity and preeclampsia. Until recently management options have been limited. Improved understanding of the basic pathophysiology is changing this.¹² Doppler ultrasound of the uterine artery can identify women at risk.¹¹ This study was aimed to evaluate bilateral uterine artery Doppler between 11+0 to 13+6 weeks in the prediction of pregnancies that subsequently develop preeclampsia and IUGR.

OBJECTIVE

The objectives of this study were;

Primary

To evaluate bilateral uterine artery Doppler between 11+0 to 13+6 weeks in the prediction of pregnancies that subsequently develop preeclampsia.

Secondary

To evaluate bilateral uterine artery Doppler between 11+0 to 13+6 weeks in the prediction of pregnancies that subsequently develop IUGR

REVIEW OF LITERATURE

Hypertensive disorders in pregnancy

Hypertensive disorders of pregnancy occurs in about 8-10% of pregnant women in India.¹³ In west it accounts for approximately 2-5% of all pregnancies.¹⁴

In developing countries hypertensive disorders of pregnancy accounts for 40% to 80% of maternal mortality occurring mainly as a result of inadequacy of emergency care. Fetus of preeclamptic women have a fivefold increase in mortality compared with infants without the disorder. Preeclampsia is responsible for approximately 15% of all preterm births.¹⁵ The specialized care of these premature babies place considerable strain on health care resources of developing nations.²¹

Hypertensive disorders in pregnancy are classified into four categories as recommended by National high blood pressure education program working group¹⁶ on High Blood pressure in pregnancy as Gestational hypertension, Pre eclampsia, chronic hypertension and Chronic hypertension with superimposed preeclampsia.²

Classification of Hypertensive Disorders of Pregnancy

Number of classification systems have been proposed for hypertensive disorders in pregnancy.¹⁶

In 2000, NHBPEP (National High Blood Pressure Education Programme) proposed the use of term gestational hypertension in place of Pregnancy Induced Hypertension. Hypertensive disorders of pregnancy are classified into following categories:¹⁶

1. Gestational hypertension,
2. Preeclampsia and Eclampsia
3. Chronic hypertension
4. Preeclampsia superimposed on chronic hypertension.

Hypertension in pregnancy is defined as per ACOG guidelines¹⁷ as a diastolic blood pressure of 90mmHg or higher, or a systolic blood pressure level of 140 mm Hg or higher, after 20 weeks of gestation, with or without proteinuria, in a previously normotensive, non proteinuric woman, blood pressure measured on more than one occasion at least 4 to 6 hours apart.¹⁷

Proteinuria defined as greater than or equal to 0.3 g of protein in a 24- hour urine collection.¹⁷⁻¹⁹

It has been suggested in few studies that rise in Blood pressure of 30 mm Hg systolic or 15 mm Hg diastolic should also be considered as a criteria to diagnose preeclampsia.^{18,19} But recent guidelines suggest that these patients are at increased risk of development of PIH and benefit from close observation if occurring in presence of proteinuria and hyperuricemia.^{18,19}

Gestational hypertension^{18,19}

Also referred to as “transient hypertension of pregnancy”.

1. Hypertension appearing for first time after 20 weeks of gestation.
2. Return to normal BP before 12 weeks postpartum.
3. No proteinuria or any of severe features of preeclampsia

Pre-eclampsia-eclampsia^{18,19}

1. De novo appearance of hypertension after 20 weeks of gestation
2. Proteinuria of at least 300 mg/24 hr OR
3. Any of the features as defined by ACOG criteria for Severe Preeclampsia.

Preeclampsia that manifests with convulsion is defined as eclampsia.

Features of severe pre eclampsia^{18,19}

1. Hypertension – systolic > 160 mm Hg or diastolic > 110 mm Hg on two occasions atleast 4 hrs apart while the patient is on bed rest.
2. Thrombocytopenia- platelet count < 1,00,000/microlitre
3. Impaired liver function test – elevated liver transaminases to twice the normal, severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnosis or both.
4. New development of renal insufficiency - Serum creatinine >1.1 mg/dL OR doubling of serum creatinine in absence of renal disease.
5. Pulmonary edema
6. New onset cerebral or visual disturbances
7. FGR

For management purposes both gestational hypertension and pre-eclampsia are considered as one. But prognostically gestational hypertension is better than pre-eclampsia.²⁰

Chronic hypertension^{18,19}

1. Hypertension diagnosed before 20 weeks of gestation not attributable to gestational trophoblastic disease or multiple pregnancy.
2. Hypertension persisting for more than 12 weeks after pregnancy

Preeclampsia superimposed upon existing hypertension^{18,19}

1. New onset proteinuria in hypertensive women after 20 weeks gestation.
2. Sudden increase in BP or proteinuria or thrombocytopenia in women with hypertension and proteinuria after 20 weeks of gestation.

JNC guidelines define worsening proteinuria in women with chronic hypertension as a sudden, 2-3 folds increase in proteinuria.²¹

If the woman with chronic hypertension also manifests evidence of preeclampsia, this is classified chronic hypertension with superimposed preeclampsia.^{18,19}

Diagnosis of PRE-ECLAMPSIA

The criteria that defines pre-eclampsia are: onset at >20 weeks gestational age, 24-hour proteinuria 300 mg/day¹⁹ or, if not available, a protein concentration 30 mg (1+ on dipstick) in a minimum of two random midstream urine samples collected at least 4–6 hours , a systolic blood pressure >140 mmHg or diastolic blood pressure 90 mmHg as measured twice, using an appropriate cuff, 4–6 hours apart, and disappearance of all these abnormalities before the end of the 6th week of postpartum.

Nonetheless, some presentations of hypertensive disorders of pregnancy along with clinical or laboratory abnormalities or intrauterine growth restriction should also be considered as potential pre-eclampsia.²²

Epidemiology

Prevalence

Worldwide

Pre-eclampsia is a multisystem disorder which complicates 3% to 8% of pregnancies in Western countries and contributes to a major source of morbidity and mortality worldwide.^{23,24} Overall, 10%–15% of maternal deaths are associated with pre-eclampsia and eclampsia.^{24,25}

India

The prevalence of hypertension during pregnancy is not well-documented in Indian literature and the studies related to hypertension in pregnancy in India were mostly hospital based.

The prevalence of hypertension during pregnancy was found to be 6.9% in a rent study by Mehta B et al.²⁶ in Community Health Center (CHC) Chiri, Block Lakhanmajra, Haryana. Sachdeva et al.,²⁷ in Gujarat, reported incidence of pregnancy-induced hypertension (PIH) to be 15% among women of rural background. In a population-based study carried out by Sayeed et al.,²⁸ in a rural community of Bangladesh, prevalence of systolic and diastolic hypertension was reported as 6.8 and 5.4%, respectively.

Major risk factors for pre-eclampsia²⁹

Risk factor	OR or RR (95% CI)
Antiphospholipid antibody syndrome	9.7 (4.3–21.7)
Renal disease	7.8 (2.2–28.2)
Prior pre-eclampsia	7.2 (5.8–8.8)
Systemic lupus erythematosus	5.7 (2.0–16.2)
Nulliparity	5.4 (2.8–10.3)
Chronic hypertension	3.8 (3.4–4.3)
Diabetes mellitus	3.6 (2.5–5.0)
High altitude	3.6 (1.1–11.9)
Multiple gestations	3.5 (3.0–4.2)
Strong family history of CV disease (heart disease or stroke in 2 first-degree relatives)	3.2 (1.4–7.7)
Obesity	2.5 (1.7–3.7)
Family history of pre-eclampsia in first-degree relative	2.3–2.6 (1.8–3.6)
Advanced maternal age (>40 years)	1.68 (1.23–2.29) for nulliparas 1.96 (1.34–2.87) for multíparas

CI, confidence interval; OR, odds ratio; RR, relative risk; CV, cardiovascular.

Other risk factors have been identified, including a medical history of chronic hypertension, kidney disease, diabetes, obesity, birthplace in Africa, age > 35 years, and pregnancy characteristics, such as twin or molar pregnancy, previous pre-eclampsia, or fetal congenital abnormality.^{30,31} High altitude has also been shown to

increase the incidence of pre-eclampsia, and is attributed to greater placental hypoxia, smaller uterine artery diameter, and lower uterine artery blood flow.³²

Pathophysiology

Role of trophoblast invasion

During normal pregnancy, the villous cytotrophoblast invades into the inner third of the myometrium, due to which spiral arteries lose their endothelium and most of their muscle fibers. These structural modifications are associated with functional alterations, such that spiral arteries become low-resistance vessels, and thus less sensitive to vasoconstrictive substances.²⁵

Pre-eclampsia has a complex pathophysiology, the primary cause being abnormal placentation. Placental remodelling occurs in two stages. In the first stage, between 8 and 12 weeks' gestation, trophoblastic cells invade the intradecidual portion of the spiral arteries. This is followed by deeper trophoblastic invasion into the myometrial segments of the spiral arteries from 14 weeks' gestation. The loss of smooth muscle and elastica from the spiral arteries converts the uteroplacental circulation into a low resistance, high capacitance system.^{33,34} Placental remodeling is completed by 16–18 weeks' gestation.³⁵

Defective placental implantation leads to hypoperfusion, hypoxic reperfusion injury, and oxidative stress. A derangement in trophoblastic differentiation is thought to underlie the pathophysiology of gestational hypertension, preeclampsia, and fetal growth restriction (FGR). Defective implantation may also play a causative role in preterm labour, placental abruption, and second-trimester miscarriages. Recent studies indicate that poor placentation is associated with an imbalance of circulating

vasoactive factors and, in turn, leads to maternal vascular maladaptation with associated systemic endothelial dysfunction. Placental products are released as part of the placentation process. Levels of these biochemical markers reflect the pathophysiology of defective placentation, and, as a consequence, have assumed an increasing role in early gestation screening tests for later pregnancy complications. These biomarkers include pregnancy-associated plasma protein-A (PAPP-A), placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin (sEng), activin-A, and inhibin-A.³⁵

Oxidative stress, lipid peroxidation and preeclampsia

Placental oxidative stress is a state of placental damage caused by reactive oxygen species. Prooxidants include free radicals and other reactive oxygen species. Antioxidants are compounds and reactions that dispose and suppress actions of reactive oxygen species.³⁸

Reduced placental perfusion as a result of abnormal placentation and failure of the trophoblast to invade the maternal spiral arteries leads to ischemia reperfusion injury resulting in the release of oxidative molecules.³⁹

This condition promotes lipid peroxidation and the endothelial cell dysfunction that may play important roles in pathophysiology of preeclampsia or intra-uterine growth retardation.⁴⁰

However, it has been unclear whether oxidative stress is a stage in the disease process or a cause of preeclampsia.⁴¹ Several multi-center randomized clinical trials using antioxidants for prevention of preeclampsia are currently underway and the findings have been mixed.⁴²

Endothelial dysfunction

Endothelial cell dysfunction, which possibly results from abnormal placentation and placental development, oxidative stress, and the potential interaction between these factors with maternal response, could be responsible for all the clinical aspects of the maternal syndrome of preeclampsia including hypertension, proteinuria, and edema.^{39,41}

These changes result in increased peripheral vascular resistance, changing in the modulation of vascular tone, excessive vasoconstriction in the small arterioles in the uteroplacental compartment as well as other systemic vascular beds.^{41,42}

Endothelial dysfunction was a potential contributory factor in the hypothetical pathway for the development of preeclampsia.⁴³

Other hypothetical mechanisms and biological changes

Some other mechanisms (immune maladaptation, genetic susceptibility, and lipid metabolism) and factors (pro-angiogenic and anti-angiogenic, and predisposing maternal factors) may play a role in the development of preeclampsia.

Genetic susceptibility

There is a hypothesis that development of preeclampsia/eclampsia may be based on a single recessive gene or a dominant gene with incomplete penetrance from contributions of maternal and fetal genes, or an interaction between maternal and fetal genotypes.^{41,44}

Proangiogenic and anti-angiogenic factors

. Some angiogenic factors has been investigated including high serum levels of soluble fms-like tyrosine kinase 1 (sFlt1), an anti-angiogenic protein, and low levels of placental growth factor (PlGF), a pro-angiogenic protein.⁴⁵

Role of predisposing maternal factors

Several maternal constitutional factors may increase the risk of preeclampsia or increase maternal susceptibility to preeclampsia. These include diabetes, hypertension, obesity, and hyperlipidemia.⁴¹

Fetal Growth Restriction (FGR) / Small for gestational age (SGA)

Fetal growth is a useful marker for fetal well-being [56, 57]. Pregnancies complicated by intrauterine growth restriction (IUGR), defined as a pathological process of reduced fetal growth, have been associated with an increase in perinatal mortality [58, 59]. SGA are those infants whose birth weights are below the tenth centile for their gestational age. Preeclampsia is a significant risk factor in the development of FGR and represents the most common cause of FGR in the non-anomalous infant. Data has consistently shown that for any given gestational age at birth, including term, a weight below the 10th percentile significantly increases the risk of mortality.⁴⁶ Hence, an infant at 38–40 weeks with a weight of 1,250 grams has a significantly greater mortality risk than one born of similar weight at 32 weeks.⁴⁷ It is important to note that while reduced birth size is associated with severe preeclampsia, it has not been as well described in pregnancies complicated by mild preeclampsia.⁴⁸

Ødegård et al.⁴⁹ showed pregnancies complicated by severe preeclampsia had infant birth weights 12% lower than expected, while pregnancies with mild preeclampsia showed no difference in weight gain from expected norms.⁴⁹ Fetal growth restriction (FGR) that develops in the absence of preeclampsia may also have its origin in defective placentation. It has far reaching consequences: affected infants have an increased risk of coronary artery disease, hypertension, stroke, and diabetes in adulthood, in addition to increased rates of short-term morbidity and mortality.³⁵

However, the high risk of complication related to preterm delivery in the late-preterm infant, as well as the apparent negligible effect of mild preeclampsia on fetal growth and maternal health, highlight the importance of carefully selecting the appropriate time of delivery in pregnancies complicated by FGR.⁵⁰

Prediction of hypertensive disorders of pregnancy

A variety of biological, biochemical and biophysical markers implicated in pathophysiology of preeclampsia have been proposed to predict its development. Despite decades of research, the ability of clinicians to predict preeclampsia presymptomatically has not improved remarkably. Patients suffering early onset preeclampsia have significant maternal and perinatal morbidity and mortality.⁵¹

There is a need for screening test which is widely applicable and affordable and it helps in presymptomatic diagnosis for timely identification and monitoring of at risk patients and thus providing the best prenatal care for these women and their child. For a screening test to be effective it should be adequately sensitive, specific, and have good positive predictive value. Furthermore when evaluating these new tests, cost, patients acceptability, and quality control should be taken into account.⁵²

Fulfilling these criteria several tests have been described either alone or in combination. But this data comes on the background of small case studies/trials.^{53,54}

The biochemical tests performed commonly are;

- PAPP-A (Pregnancy associated plasma protein A) with a sensitivity of 5%
- PIGF (placental growth factor)
- B-hcg
- Doppler

These biochemical markers combined with uterine artery PI at 11-13⁺⁶ weeks could approximately identify 90% , 80% and 60% of pregnancies that subsequently develop early (<34 weeks) , intermediate (34-36weeks) and late (>37weeks) PE at false positive rate of 5%.

Other tests include :

1. Provocative tests^{53,54,18,19,20}

These tests are evaluated to assess blood pressure increase in response to a stimulus

A. Isometric hand grip exercise test.

B. Roll over test (Gant's roll over test):

C. Angiotensin infusion test (invasive test):

None of these tests are currently being used clinically because they are cumbersome, expensive, time-consuming, invasive and most important unreliable. Sensitivities of all these tests varies from 55 to 70% with specificities of 85%.¹⁸⁻²¹

Laboratory tests

- Urinary calcium excretion
- Urinary soluble endoglin
- Urinary proteomics
- Urinary inhibin A.
- Urinary Kallikrein – Creatinine Ratio (Uk:Cr)
- Clinical value of microtransferrinuria and microalbuminuria
- Urinary excretion of N-acetyl-beta-glucosaminidase
- Serum Inhibin A
- Maternal serum alpha fetoprotein (MSAFP)
- SERUM TNF LEVELS
- Coagulation Factors and Platelets
- Plasma fibronectin
- Serum thrombomodulin
- Serum androgen markers and Sex Hormone Binding Globulin (SHBG) markers
- Serum CA125 variability- -new aspects of clinical usefulness
- Lipoprotein a-Lp (a)
- Angiogenic factors in preeclampsia
- sFlt1
- Combined PLGF/sFlt1 ratio

- Fetal Erythrocytes in Maternal Blood
- Serum collagen levels
- Amniotic fluid cytokinase
- ADAM 12
- Placental protein 13
- Pentraxin 3 (PTX 3)
- Visfatin
- Adrenomedullin

Doppler ultrasound

Doppler velocimetry is a noninvasive technique which uses high frequency sound waves for evaluation of blood flow. It depicts the state of uteroplacental blood flow from which condition about fetal condition and probability of developing pre-eclampsia can be made.^{55,56}

Doppler ultrasonography of the uterine arteries

The underlying mechanism for development of preeclampsia is thought to be incomplete trophoblastic invasion of spiral arteries. The inadequate placental perfusion has lead to the use of Doppler ultrasonography to assess the velocity of the blood flow in the uterine arteries.^{55,56}

Uterine artery Doppler at 11-13⁺⁶ weeks can be used to predict the women destined to develop preeclampsia. An abnormal uterine artery waveform is characterized by pulsatility index above 95th percentile or the presence of early diastolic notching unilaterally or bilaterally.⁵⁵

Uterine artery Doppler velocimetry has a sensitivity of 20-60% and specificity of 80-90%. But this test is not widely available and requires expertise to perform.^{53,54}

Among high-risk patients with a previous preeclampsia, Doppler ultrasound of the uterine arteries has an excellent negative predictive value.⁵⁷

However, several studies have shown that the measurement of uterine perfusion in the second trimester and analysis of angiogenic markers have a high detection rate especially for early onset preeclampsia.^{58,59}

Prediction of pre-eclampsia by Doppler ultrasound and serum biomarkers⁶⁰⁻⁶⁵

	1 st trimester			2 nd trimester			
	PE	EO PE	LO PE	PE	EO PE	LO PE	LO PE
Doppler ultrasound							
Uterine artery diastolic flow	↓			↓			
Uterine artery pulsatility index	↑			↑			
Uterine artery resistance index	↑			↑			
Biochemical markers							
Activin A	↑			↑	↑		
Inhibin A	↑			↑	↑		
A disintegrin and metalloproteinase 12 (ADAM12)	↓/↔				↔		
Free β subunit of hCG (hCGβ)	↔			↑/↔			
Human chorionic gonadotropin (hCG)	↔				↑/↔		
Pregnancy-associated plasma protein-A (PAPP-A)	↓	↓	↓	↓			
Placental protein 13 (PP13)	↓	↓					
Placental growth factor (PlGF)	↓/↔	↓/↔	↓/↔	↓	↓	↓	
Soluble endoglin (sEng)	↔			↑	↑		
Soluble vascular endothelial growth factor receptor 1 (sVEGFR-1)	↔	↔	↔	↑	↑	↑	

PE = preeclampsia; EO= Early onset; LO= Late onset Arrows indicate the Doppler ultrasound findings or changes in the concentrations of the respective biomarkers in women who developed pre-eclampsia as compared to controls (↑ elevated, ↓ decreased, ↔ no change).

Flow velocity waveform from uterine artery in a non-pregnant woman and a pregnant woman

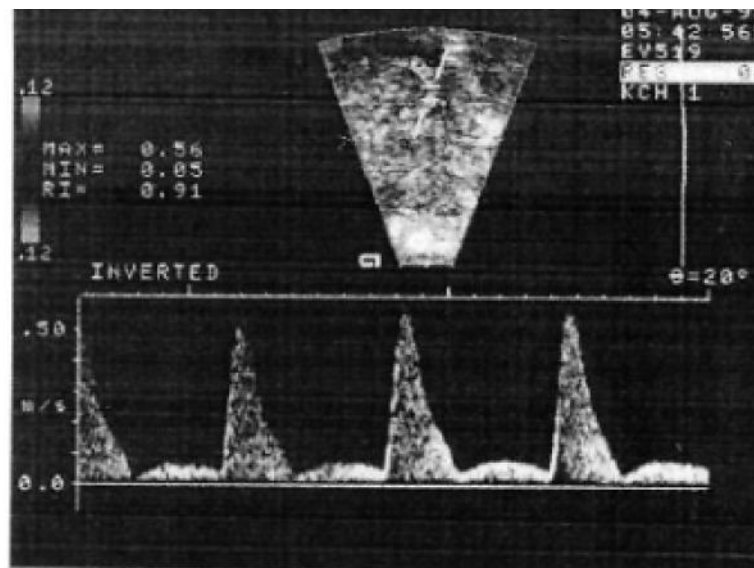


Figure 1. Flow velocity waveform (FWW) of uterine artery in a non pregnant patient: Characteristics shape of this waveform shows a steep systolic slope, an early diastolic notch and a small amount of diastolic flow.

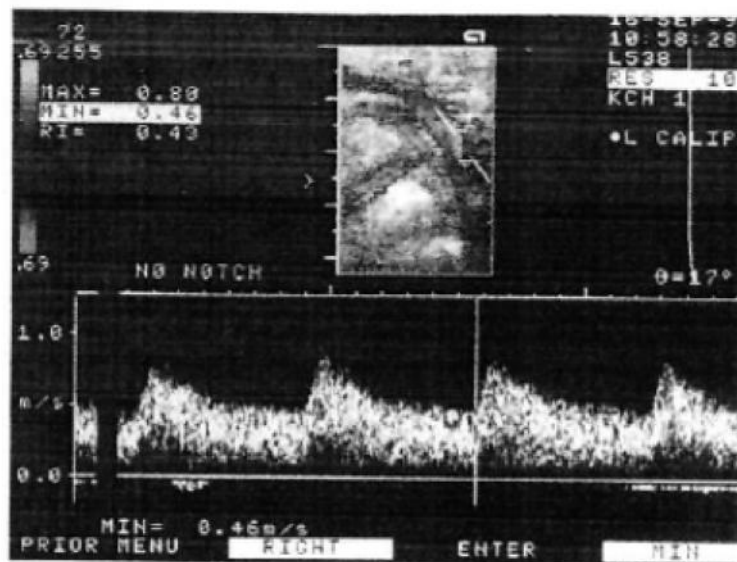


Figure 2. FWW in established pregnancy at 20 weeks: Placentation typically results in a low resistance FWW, the disappearance of the notch and an abundance of diastolic flow

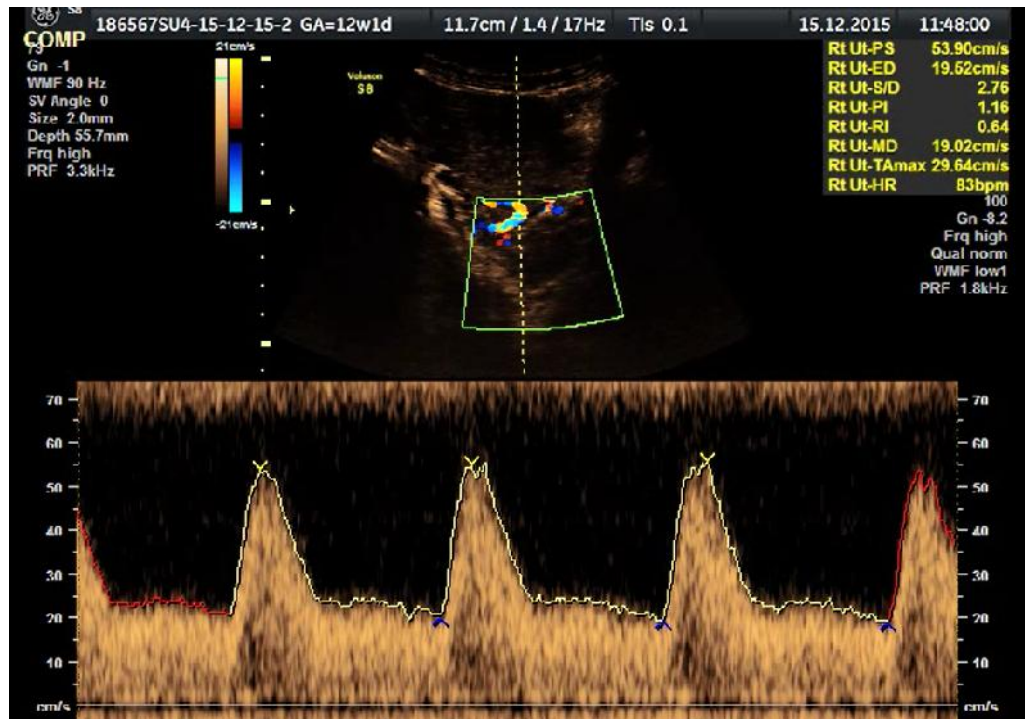


Figure 3. FWV in pregnancy at 12 weeks: Normal Doppler

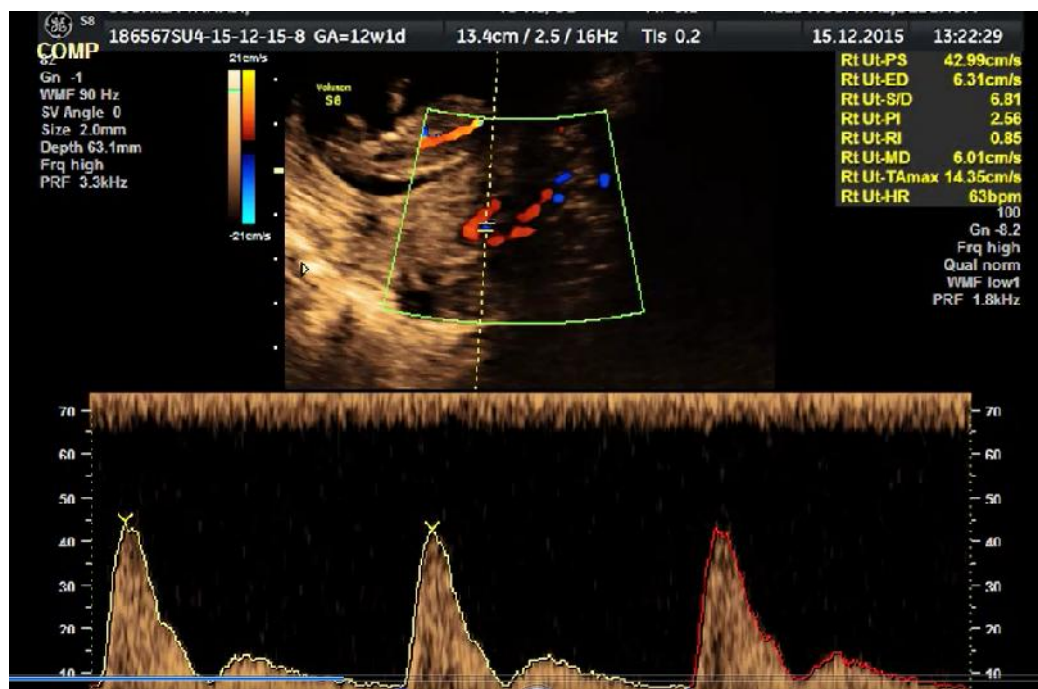


Figure 4. FWV in pregnancy at 12 weeks: Increased Resistance on Uterine Artery Doppler

Rationale of using Doppler velocimetry indices in measures of uteroplacental blood flow

Placental blood flow and degree of vascular resistance in the uteroplacental circulation can reflect current status of the fetus and predict several adverse pregnancy outcomes. It is difficult and impractical to measure directly uteroplacental circulation in human. This leads to the development of surrogate sensitive, safe, and noninvasive measures, such as Doppler ultrasound of the uterine artery.⁶⁶

Multiple publications have reviewed the utility of Doppler studies of the uterine artery and umbilical artery as a test for prediction of the onset of preeclampsia and other pregnancy outcomes.⁶⁷⁻⁷²

Persistent abnormalities in the uterine artery Doppler waveform at 12-20 weeks of gestation can reflect inadequate placental development and an increased risk of developing preeclampsia.^{39,41}

Doppler indexes of the uterine artery can be used for the prediction of intrauterine growth retardation, hypertensive disorders of pregnancy, cesarean section for fetal distress, meconium, fetal asphyxia, admission to the neonatal intensive care unit, and perinatal mortality.^{71,73}

Although no single marker is currently adequate to predict the development of preeclampsia, uterine artery Doppler velocimetry at mid-gestation is considered a very sensitive predictor for the development of preeclampsia, and some authors stated that it would currently be the best predictive test,⁷⁴⁻⁷⁶ especially in combination with some other biomarkers for endothelial and placental function (e.g. PAI-1/PAI-2 ratio, leptin, placental growth factor).⁷⁵

Doppler flow velocity waveform indices in uterine and umbilical artery

Doppler ultrasound in medical imaging consists of a continuous wave Doppler (CW), pulsed wave Doppler (PW), and color Doppler imaging (CDI). When ultrasound is reflected from movements of a target, such as red blood cells, the frequency shift of the targets will be detected. The final Doppler signal displayed on the monitor is a waveform representing the Doppler shifts created by circulating red cells during a cardiac cycle. In a typical and normal shape of flow waveform, several measures are presented in Figure.

Flow velocity waveforms (FVW) with measures

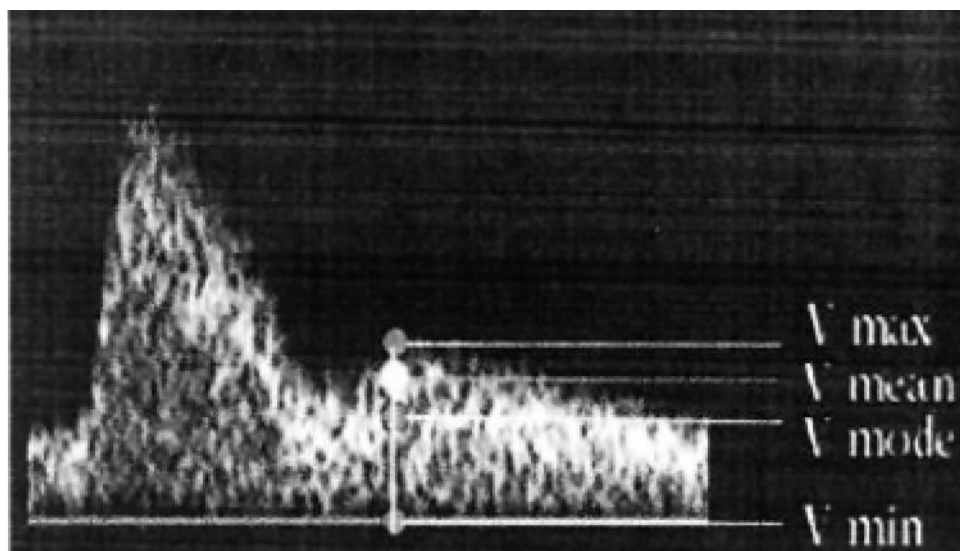


Figure 5. Flow velocity waveform of the uterine artery with mode, mean, minimum (min) and maximum (max) velocity (V)

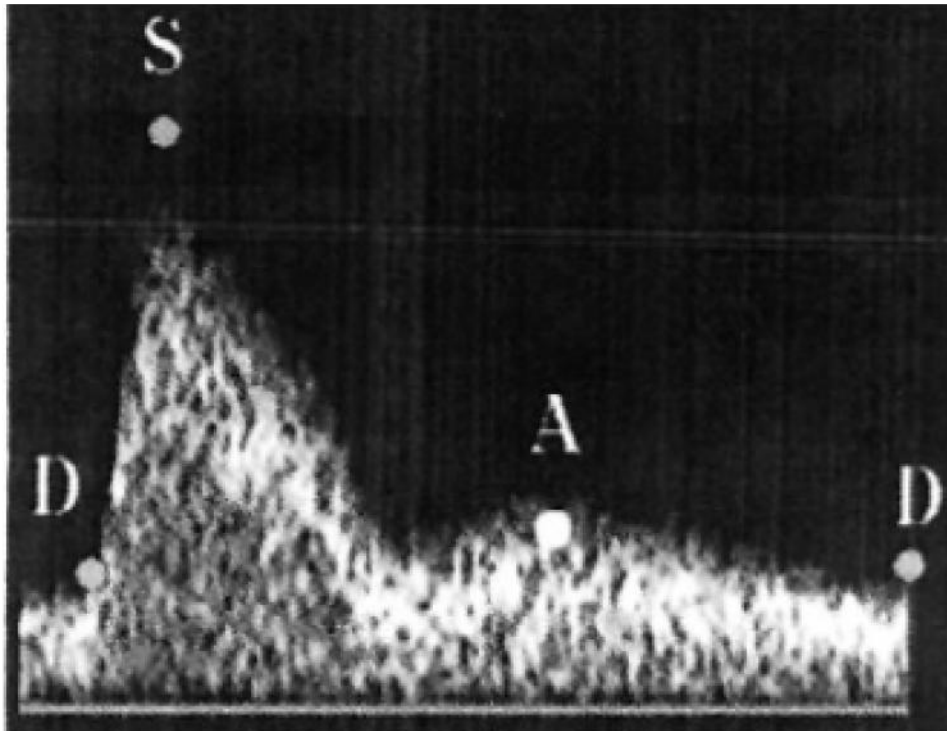


Figure 6. Flow velocity waveform with S (maximum peak systolic frequency D (end-diastolic velocity) and A (mean Doppler shift frequency)

S: maximum peak systolic frequency

D: end-diastolic frequency

A: mean Doppler shift frequency during a cardiac cycle

Resistance Index(RI) =

(Peak systolic height – Minimum diastolic height)/ peak

systolic height = (S-D)/S

As diastolic falls, the value of the RI increases, if there is no diastolic flow, the RI=1.

RI values greater than 1 are possible, if there is reversed diastolic flow.

Pulsatility index

Pulsatility index (PI) = (Peak systolic height – Minimum diastolic height)/Mean waveform height = (S-D)/Mean or (S-D)/A

PI and RI directly reflect the downstream flow impedance. PI may be more informative than RI since PI takes the entire waveform into account and not just the maximum and minimum frequencies, as does RI.

S/D ratio –

Systolic/Diastolic Ratio (A/B ratio, S/D ratio) = S/D: as diastolic falls, S/D increase, when there is no diastolic flow, the S/D ratio is infinity. Given the absent end-diastolic flow velocity, S/D will not be measurable.

Early diastolic notch:

Because of trophoblast invasion, in the uterine artery flow velocity waveform the diastolic notch gradually disappears during early second trimester. By 20 weeks of pregnancy, the majority of women have low resistance uterine artery FVWs with 20% retaining a notch in either uterine artery FVW. At 24 weeks the number of women with notching is 9%.

A high-amplitude wave from the placental bed can result from increased uteroplacental circulation, which produces a notch in the uterine artery Doppler during diastole. A number of studies found that when an early diastolic notch is noted, irrespective of its depth in relation to peak systolic flow, the woman was considered at risk for developing preeclampsia. These studies used notching as only one index for abnormal uterine artery Doppler measures.^{39,77}

Reverse flow at the end of diastole:

A substantial increase in the vascular resistance of the uteroplacental unit leads to a decrease in end-diastolic flow velocity or its absence in the FVW, even reverse flow at the end of diastole appears.

Time for applying Doppler ultrasound for the prediction of preeclampsia

Previous studies used uterine artery Doppler examination at different times during pregnancy for the prediction of preeclampsia and hypertensive disorders during pregnancy. The predictive values of the Doppler as a screening test (sensitivity, specificity, positive predictive value, and negative predictive value) change as gestational age increases. Several studies applied the test at around 20 weeks' gestation.⁷⁸

Others have applied it at around 24 weeks' gestation^{71,79} or anytime during second trimester at 16-28 weeks' gestation.⁶⁷

Testing women at around 20 weeks may produce higher false positive result for the test,^{77,78} but it is also very good time to routinely perform scan for fetal anomalies. Performing the test at 28-32 weeks' gestation has highest predictive value,⁷⁸ but it is too late to apply prophylactic treatment to modify the disease.⁷⁸

Some researchers performed the test at early pregnancy at 11-14 weeks' gestation⁶⁸ and found uterine artery PI at early pregnancy can be predictive for the disease. By performing Doppler at 11-13⁺⁶ weeks, timely pharmacological intervention for prevention of pre-eclampsia can be done.

Uterine artery Doppler for the prediction of preeclampsia.

Although a reliable method of measuring placental blood flow directly is not available at present, the uterine artery Doppler velocimetry is a good alternative by enabling detection of high uterine vascular resistance attributable to inadequate uteroplacental blood circulation in preeclampsia.⁸⁰

High impedance in the uterine arteries in preeclampsia, presented by high resistance index value along with the persistence of an early diastolic notch, can be detected by Doppler ultrasound.

A number of studies with varying results (sensitivity, specificity, positive predictive value, and negative predictive value) have been published.^{67,74,,77,78}

This variation can be explained, in part, because of differences in the timing, site, and evaluation of Doppler studies, by the different equipment used or techniques, by small number of patients, varying sampling sites, different gestational age of participants, as well as different criteria for the classification of Doppler indices. The different cutoff levels used for Doppler indices in studies have lead to vary the results, for example the cut-points for RI varied from 0.52 – 0.62.

Doppler indices can be categorized into quantitative measures (Pulsatility Index, Resistance Index, S/D ratio) or qualitative measures (early diastolic notch, reverse diastolic flow). The value of quantitative assessment can be assessed in either absolute measures (specific cut-point at specific gestational age) or relative measures (based on percentile of the value distribution in the study population).

In clinical screening for preeclampsia, the early diastolic notch has a high specificity and negative predictive value, but a poor sensitivity and positive predictive value.³⁹

In unselected women, the presence of a diastolic notch is reported to perform better in predicting preeclampsia than an elevated resistance index^{67,79} or systolic/diastolic ratio.⁷⁹ However, a large, multi-centre observation study,⁷² found that mean PI performs better than early diastolic notching in predicting preeclampsia.

In a meta-analysis, Goffinet et al⁸¹ found no significant difference between the Doppler and control groups for antenatal hospitalization, obstetric outcome or perinatal morbidity in unselected and low risk population.

Other studies^{82,83} have confirmed the significant role of abnormal umbilical Doppler velocimetry (absent end-diastolic flow, S/D ratio greater than 3.0) in prediction of adverse perinatal outcomes.

Studies evaluating role of bilateral uterine artery Doppler in predicting preeclampsia and IUGR

Martin AM et al.⁸⁴ in 2001 conducted a study to examine the value of uterine artery Doppler at 11-14 weeks of gestation in the identification of women at risk of developing pre-eclampsia and fetal growth restriction. The authors carried out uterine artery Doppler at 11-14 weeks in 3324 consecutive singleton pregnancies attending for routine care in three London hospitals. The right and left uterine arteries were identified using color flow mapping and velocity waveforms were obtained using pulsed Doppler. The mean pulsatility index of the two arteries was determined and the predictive value of a mean pulsatility index > the 95th centile in the prediction of pre-

eclampsia and/or fetal growth restriction was calculated. The results showed that, satisfactory flow velocity waveforms were obtained from both uterine arteries in 3195 (96.1%) of the 3324 pregnancies examined and complete outcome information was obtained for 3045 (95.3%) of these women. The 95th centile of the uterine artery mean pulsatility index was 2.35 and did not change significantly with gestational age. The pregnancy was complicated by pre-eclampsia in 63 (2.1%) cases and by fetal growth restriction in 290 (9.5%) cases. The sensitivity of a mean pulsatility index > 2.35 for pre-eclampsia (with or without fetal growth restriction) was 27.0% but for fetal growth restriction alone it was 11.7%. The respective sensitivities for these complications requiring delivery before 32 weeks of gestation were 60.0% and 27.8%, respectively. The study concluded that, uterine artery Doppler at 11-14 weeks of gestation identifies a high proportion of women who develop severe pre-eclampsia and/or fetal growth restriction.⁸⁴

Gomez O et al.⁸⁵ in 2005 carried out a prospective study to establish reference values for the first-trimester uterine artery (UtA) pulsatility index (PI) and to investigate the role of UtA Doppler in the early prediction of hypertensive disorders and their associated complications in an unselected Mediterranean population. A total of 1091 consecutive singleton pregnancies undergoing routine early ultrasound screening at 11-14 weeks of gestation was performed. The left and right UtA were examined by color and pulsed Doppler transvaginally. The mean PI and the presence of bilateral protodiastolic notching were cross-sectionally recorded. Reference ranges were calculated and the pregnancies were followed for occurrence of pre-eclampsia, gestational hypertension, intrauterine growth restriction, placental abruption and stillbirth. The sensitivity and predictive values of a mean UtA-PI > 95 th percentile and the presence of bilateral notching in the prediction of these pregnancy complications

were calculated. A total of 999 women were finally included. Both the mean UtA-PI and the prevalence of bilateral notches showed a significant linear decrease between 11 and 14 weeks' gestation. Sixty-seven (6.7%) pregnancies developed at least one of the formerly described complications, including 22 (2.2%) cases of pre-eclampsia and 37 (3.7%) cases with intrauterine growth restriction. Compared with women with a normal outcome, complicated pregnancies showed a significantly higher mean PI (2.04 vs. 1.75; $P < 0.05$, t-test) and a higher prevalence of bilateral notching (58% vs. 41%; $P < 0.05$, Chi-square test). Using the 95th percentile in mean UtA-PI as a cut-off, 23.9% (95% CI, 13.7-34.1) of complicated pregnancies and 30.8% (95% CI, 5.68-55.85) of severe cases were identified. This study showed that, pregnancies with an increased risk of developing hypertensive disorders and related complications already have an abnormally increased UtA-PI in early pregnancy. However, the use of a single uterine Doppler measurement for screening purposes in unselected early pregnancy populations has limited clinical value. The use of UtA-PI combined with other screening tests needs to be determined by further investigation.⁸⁵

Poon et al.⁸⁶ in 2009 investigated the role of uterine artery Doppler in the development of a predictive model for prediction of early preeclampsia. The detection rates for early preeclampsia, late preeclampsia, and gestational hypertension achieved by a model incorporating clinical history (history of preeclampsia, chronic hypertension, and method of conception) and maternal demographics (age, BMI, and ethnicity) alone were 47%, 41%, and 31%, respectively, at a 10% false positive rate.⁸⁶

Pilalis A et al.⁸⁷ in 2001 conducted a prospective study to assess the role of maternal demographic characteristics, uterine artery Doppler velocimetry, maternal serum pregnancy-associated plasma protein-A (PAPP-A) and their combination in

screening for pre-eclampsia and small-for-gestational age (SGA) fetuses at 11-14 weeks. A total of 878 consecutive women presenting for a routine prenatal ultrasound examination at 11-14 weeks were subjected to pulsed wave doppler was then used to obtain uterine artery flow velocity waveforms and the mean pulsatility index (PI) of the uterine arteries was calculated. Maternal serum samples for PAPP-A were assayed. Along with maternal history, these measurements were compared in their ability to predict adverse outcome, defined as pre-eclampsia and/or SGA and/or placental abruption. Mean uterine artery PI \geq 95(th) centile and PAPP-A \leq 10(th) centile each predicted 23% of the women that developed pre-eclampsia and 43% of cases of placental abruption. For SGA \leq 5(th) centile, mean uterine artery PI \geq 95(th) centile predicted 23% of cases and PAPP-A \leq 10(th) centile predicted 34%. Independent predictors for subsequent development of pre-eclampsia were increased mean uterine artery PI \geq 95(th) centile (OR, 2.76; 95% CI, 1.11-6.81) and maternal history of pre-eclampsia/hypertension (OR, 50.54; 95% CI, 10.52-242.73). The predicting factors for SGA \leq 5(th) centile were increased mean uterine artery PI \geq 95(th) centile (OR, 2.0; 95% CI, 1.07-3.74) and low PAPP-A (OR, 0.43; 95% CI, 0.20-0.93). Increased uterine artery PI was the only independent factor in the prediction of placental abruption (OR, 8.49; 95% CI, 2.78-25.94). The combination of uterine artery PI and maternal history of pre-eclampsia/hypertension was better than was using uterine artery Doppler alone in predicting pre-eclampsia. Similarly, for the prediction of SGA \leq 5(th) centile, combining uterine artery Doppler and maternal serum PAPP-A was better than was uterine artery Doppler alone. In both cases, the difference approached statistical significance. The study concluded that, the combination of maternal history with abnormal uterine artery

Doppler and low PAPP-A level at 11-14 weeks achieves better results than does either test alone in the prediction of pre-eclampsia and SGA.⁸⁷

Schulman and colleagues⁸⁸ determined that in the non pregnant state there is a rapid rise and fall in uterine artery flow velocity during systole and a “notch” in the descending waveform in early diastole. 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.⁸⁸

K. Harrington et al.⁸⁹ studied trans-vaginal uterine and umbilical artery Doppler at 10 - 12 weeks of gestation, measuring early diastolic notch, resistance index, pulsatility index and subsequent development of pre- eclampsia and IUGR, concluded that abnormal doppler value leads to Pregnancy Induced Hypertension (PIH), premature delivery and Small for Gestational Age (SGA) baby.

Sahoo K. et al.⁹⁰ in 2014 conducted a prospective study to determine the role of uterine artery Doppler flow velocimetry at second trimester of pregnancy in prediction of preeclampsia. This study was carried out in the Krishna institute of Medical science, Karad. The study included 220 pregnant women (primigravida) from August 2013 to September 2014 whose Uterine artery resistive index and pulsatility index was calculated between 14 to 20 weeks of pregnancy. The main uterine artery was located at the uterocervical junction close to the cross- over point of the uterine and external iliac arteries on both sides. $RI > 0.7$ & $PI > 1.4$ was considered abnormal. Authors concluded that, Doppler velocimetry of uterine artery at second trimester of pregnancy can be used as a reliable screening test for prediction of preeclampsia and helps to identify women at high risk and helps to modify follow up and management.

MATERIALS AND METHODS

The present was conducted in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi.

Study design

The study design was a descriptive observational study.

Study duration and period

This study was conducted for period of one year from January 2016 to February 2017.

Place

The present study was conducted in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi, a tertiary care teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi.

Source of data

Pregnant women with gestational age 11+0 to 13+6 weeks of gestation attending antenatal checkup in the Department of Obstetrics and Gynecology, KLES Dr Prabhakar Kore Charitable Hospital and Medical Research Center, Belagavi during the study period were enrolled.

Sample size

The study was comprised of 117 pregnant women with gestational age 11+0 to 13+6 weeks of gestation.

Sampling procedure

The sample size was calculated based on the formula as below.

$$n = (Z)^2 \text{ Sen} (100 - \text{Sen}) / (L)^2 * \text{PR}$$

Where,

$$Z = \text{Constant (1.96)}$$

$$\text{Sen} = \text{Sensitivity 24\% (Based on a study by Gomez et al.}^{68})$$

$$\text{PR} = \text{Prevalence rate 15\%}$$

$$L = \text{Standard error (10\%) at 95\% confidence level}$$

Therefore,

$$n = (1.96)^2 24 * (100 - 24) / (2)^2 * 15$$

$$n = 116.78 \quad 117$$

The sample obtained from the above formula was 117. Hence a sample size of 117 was considered for the study. The 117 pregnant women with gestational age 11+0 to 13+6 weeks of gestation were selected based on the simple random sampling.

Selection criteria

Inclusion criteria

- Pregnant normotensive women attending antenatal clinic scheduled for NT scan.
- Pregnant women with gestational age 11+0 to 13+6 weeks.

Exclusion criteria

Pregnant women with;

- Missed abortion.
- Chronic hypertension.
- Multiple gestation.
- Major fetal anomalies incompatible with life.
- Not willing to participate in the study.
- Threatened abortion.

Ethical clearance

Prior to the commencement of study, the ethical clearance was obtained from the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Belagavi.

Informed Consent

The eligible women were explained about the nature of the study and a written informed consent was obtained (Annexure I).

Method of collection of data

After the enrollment demographic data, obstetric history and current pregnancy details were obtained through an interview. These women were subjected to clinical examination. The data obtained was recorded on the predesigned and pretested proforma (Annexure II).

Investigations

The selected women underwent following investigations.

- Nuchal translucency scan
- Transabdominal colour Doppler

Procedure

The gestational age was confirmed by measurement of fetal crown rump length through ultrasound..

A transabdominal ultrasound was used for Doppler assessment of uterine circulation for uterine artery indices using Voluson S8 ultrasound machine with 7.5 MHz transabdominal transducer. For this procedure the probe was placed on lower quadrants of abdomen, angled medially and colour Doppler imaging was used to localize the uterine artery at its crossing over the external artery. A minor movement of probe towards flanks, along with medial rotation shows common iliac artery and its division. As soon as internal iliac artery was identified, measurement was made at right and left angles. When three similar consecutive waveforms were seen, bilateral uterine artery PI and RI was calculated and mean PI was obtained.

The utero placental circulation was measured by various uterine artery Doppler indices that is, resistance index (RI) and pulsatility index (PI). Increased resistance to the flow in uterine artery was associated with the appearance of diastolic notch and increase in all these indices. The pregnant women with increased Doppler indices were followed upto delivery to analyse whether there is development of pre-eclampsia and gestational hypertension.

Outcome variables

The selected women were followed till delivery and monitored for the development of complications of pregnancy induced hypertension and/or fetal growth restriction.

Statistical analysis

The data obtained was coded and entered into Microsoft Excel Worksheet (Annexure III). The data was analysed using SPSS statistical software version 20.0. The categorical data was expressed as rates, ratios and proportions and continuous data was expressed as mean \pm standard deviation (SD). A probability value (p value) of 0.05 was considered as statistically significant. Following this test performance of PI was determined by calculating the sensitivity, specificity, positive and negative predictive value and diagnostic accuracy was calculated. The concordance of tests was determined by kappa statistics.

Landis and Koch criteria for agreement on kappa statistics.

Kappa Agreement

<0.0 Poor

0.0 – 0.20 Slight

0.21 – 0.60 Moderate

0.61 – 0.80 Substantial

0.81 – 1.00 Almost perfect

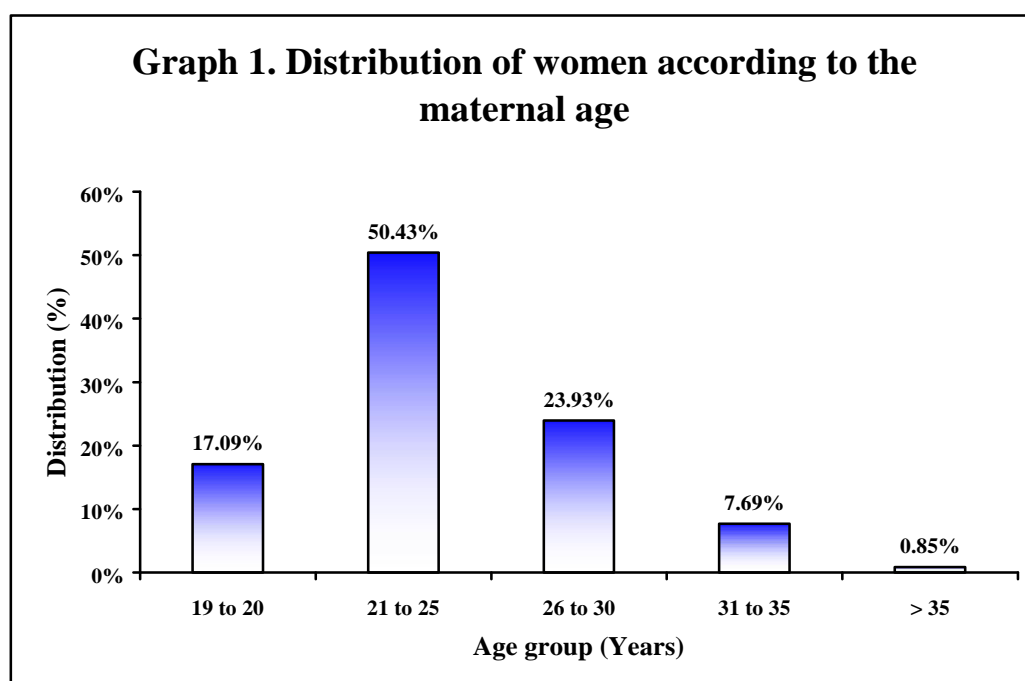
RESULTS

This one year longitudinal prospective cohort study conducted in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. The study was comprised of 117 pregnant women with gestational age 11+0 to 13+6 weeks of gestation attending antenatal checkup in the Department of Obstetrics and Gynecology, KLES Dr Prabhakar Kore Charitable Hospital and Medical Research Center, Belagavi from January 2016 to December 2016.

The data obtained was analysed and the final results were tabulated and interpreted as below.

Table 1. Distribution of women according to the maternal age

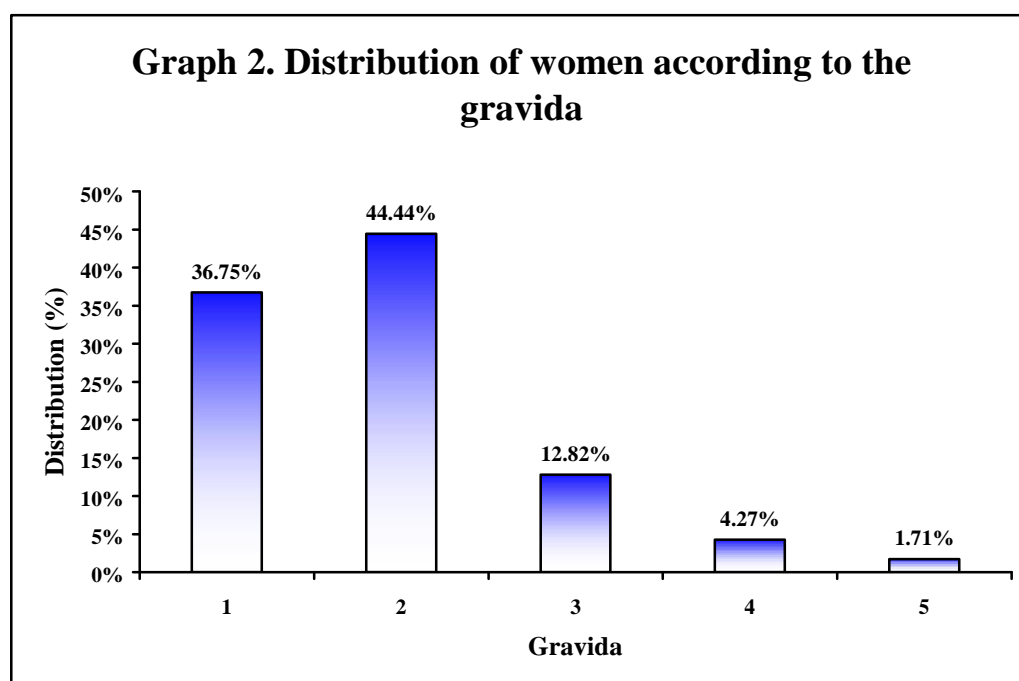
Age group (Years)	Distribution (n=117)	
	Number	Percentage
19 to 20	20	17.09
21 to 25	59	50.43
26 to 30	28	23.93
31 to 35	9	7.69
> 35	1	0.85
Total	117	100.00



In the present 50.43% of the women were aged between 21 to 25 year. The mean age was 24.41 ± 4 years. The median age was 24 years and ranged between 19 to 36 years.

Table 2. Distribution of women according to the gravida

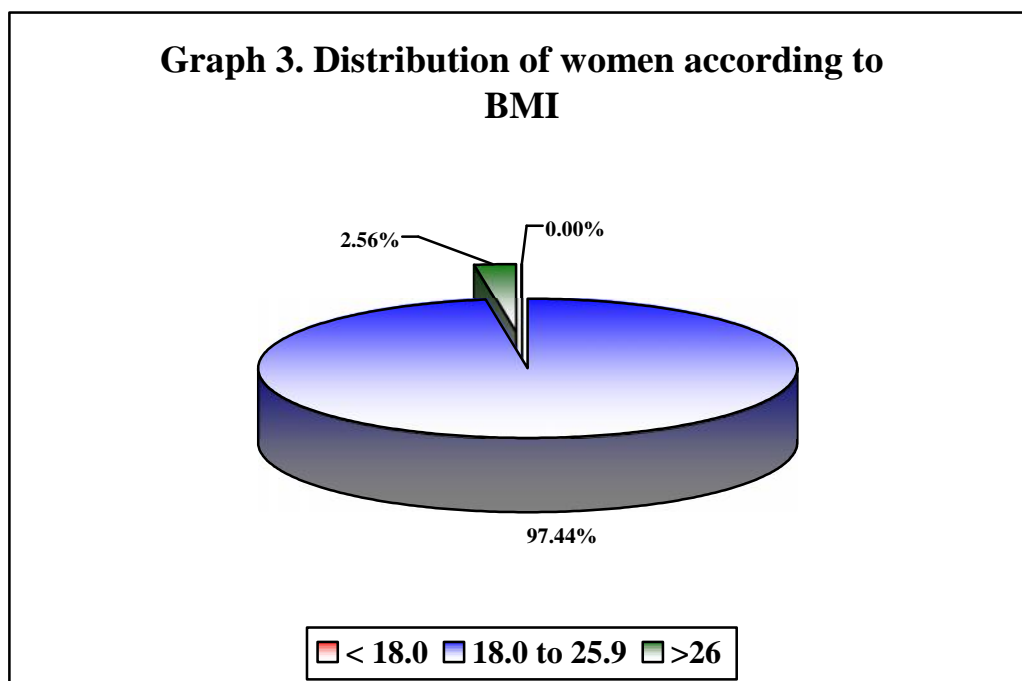
Gravida	Distribution (n=117)	
	Number	Percentage
1	43	36.75
2	52	44.44
3	15	12.82
4	5	4.27
5	2	1.71
Total	117	100.00



In this study most of the women were gravida 2 (44.44%) followed by gravida 1 (36.75%), gravida 3 (12.82%), gravida 4 (4.27%) and gravida 5 (1.71%).

Table 3. Distribution of women according to the body mass index

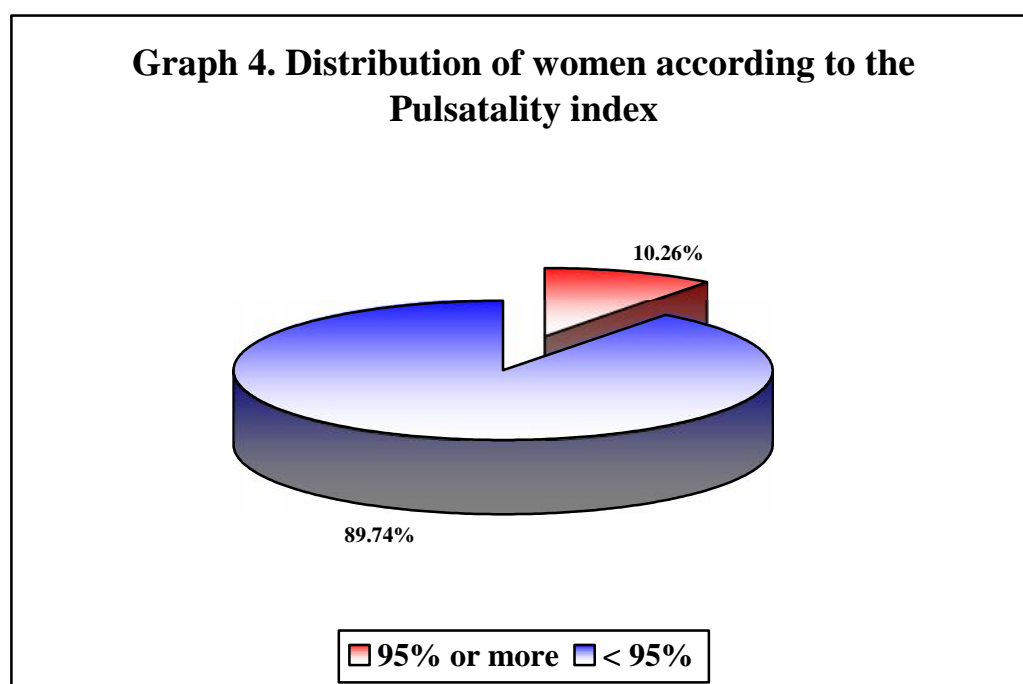
Body mass index (Kg/m ²)	Distribution (n=117)	
	Number	Percentage
< 19.80	0	0.00
19.80 to 26.0	114	97.44
> 26.0	3	2.56
Total	117	100.00



In the present study 97.44% of the women had BMI between 19.80 to 26.00 Kg/m². The mean BMI delivery was 21.91±1.6 Kg/m² and the median BMI was noted as 21.00 Kg/m² and ranged between 20 to 28 Kg/m².

Table 4. Distribution of women according to the Pulsatility index

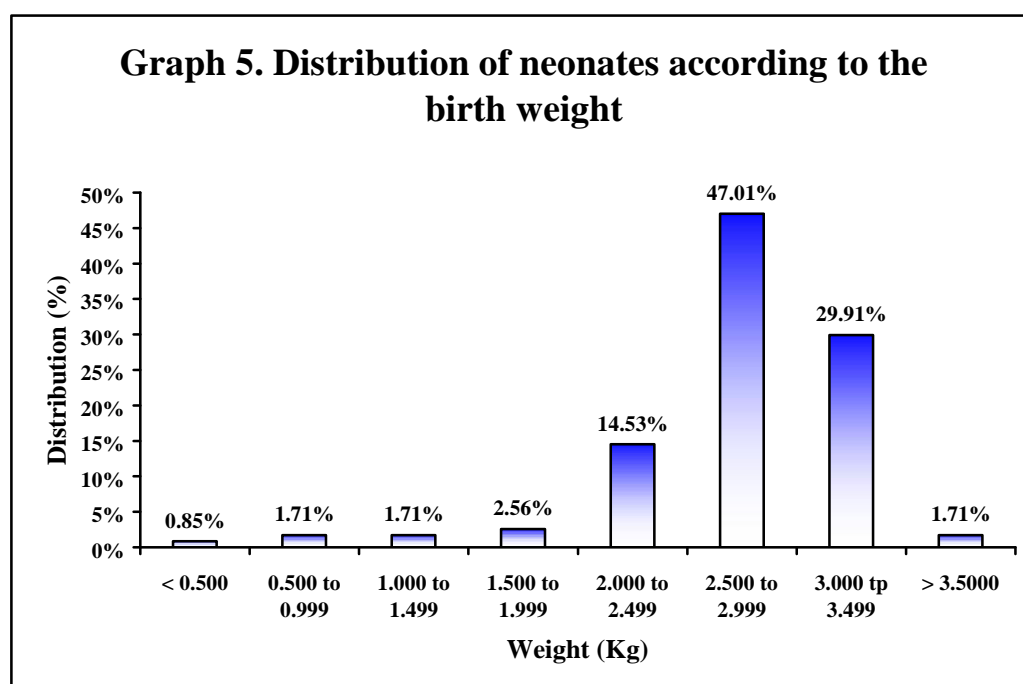
Pulsatility index	Distribution (n=117)	
	Number	Percentage
95% or more	12	10.26
< 95%	105	89.74
Total	117	100.00



In this study the pulsatility index was > 95% among 10.26% of the women and <95% among 89.74%

Table 5. Distribution of neonates according to the birth weight

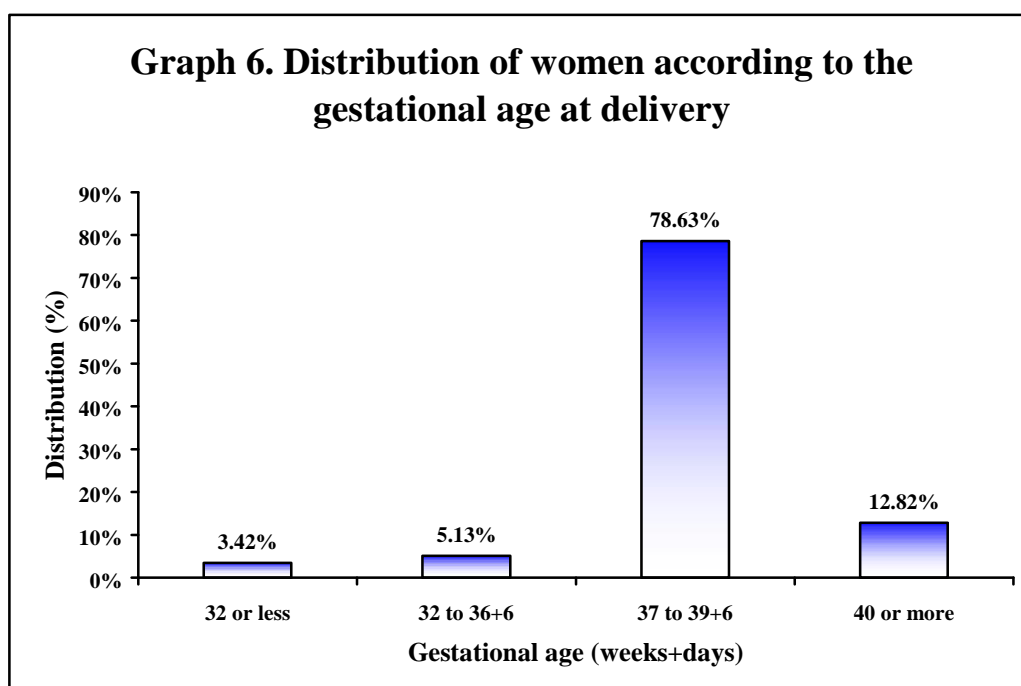
Birth weight (Kg)	Distribution (n=117)	
	Number	Percentage
< 0.500	1	0.85
0.500 to 0.999	2	1.71
1.000 to 1.499	2	1.71
1.500 to 1.999	3	2.56
2.000 to 2.499	17	14.53
2.500 to 2.999	55	47.01
3.000 to 3.499	35	29.91
> 3.5000	2	1.71
Total	117	100.00



In the present study 47.01% of the babies weighed between 2.500 to 2.999 kg followed by 3.000 to 3.499 Kg (29.91%) and 2.000 to 2.499 kg (14.53%). The mean birth weight was 2.69 ± 0.55 Kgs. and median birth weight was 2.80 Kg with range 0.1 to 4.40 Kgs.

Table 6. Distribution of women according to the gestational age at delivery

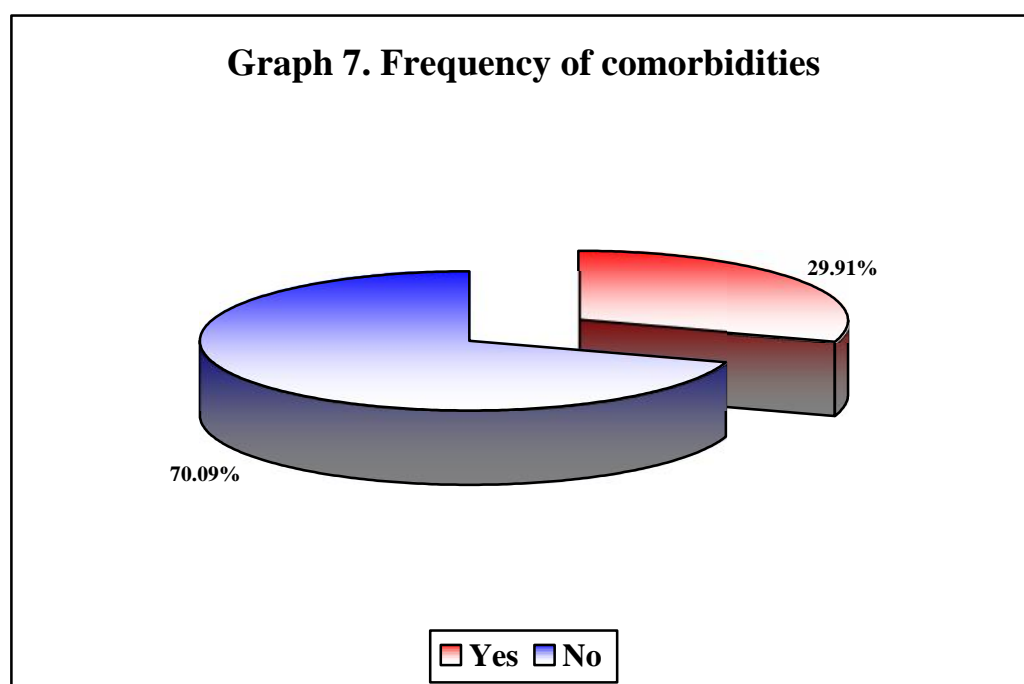
Gestational age (weeks+days)	Distribution (n=117)	
	Number	Percentage
32 or less	4	3.42
32 to 36+6	6	5.13
37 to 39+6	92	78.63
40 or more	15	12.82
Total	117	100.00



In this study most of the women delivered between 37 to 39+6 weeks (78.63%). The mean gestational age at delivery was 37.82 ± 0.55 weeks and the median gestational age at delivery was 38.29 weeks with range 21.29 weeks being minimum and 40.86 weeks being maximum.

Table 7. Frequency of comorbidities

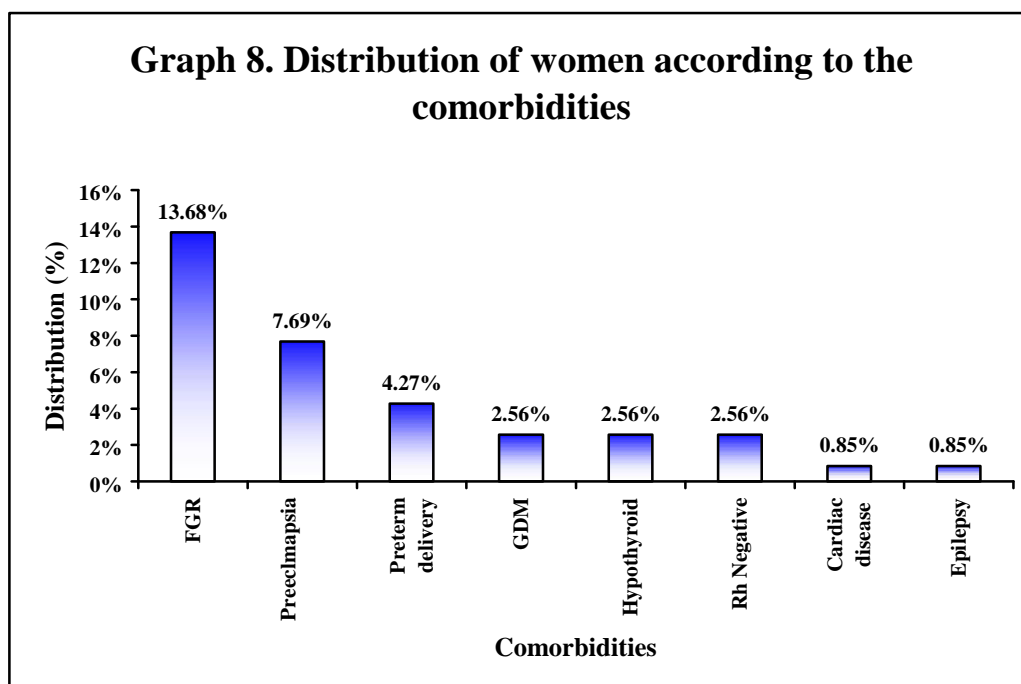
Comorbidities	Distribution (n=117)	
	Number	Percentage
Yes	35	29.91
No	82	70.09
Total	117	100.00



In this study out of 117 women, 30 (29.91%) women had comorbidities.

Table 8. Distribution of women according to the comorbidities

Comorbidities	Distribution (n=117)	
	Number	Percentage
FGR	16	13.68
Preeclampsia	9	7.69
Preterm delivery	5	4.27
GDM	3	2.56
Hypothyroid	3	2.56
Rh Negative	3	2.56
Cardiac disease	1	0.85
Epilepsy	1	0.85



In the present study most common comorbidity was FGR (13.68%) followed by preeclampsia (7.69%) the other comorbidities noted were preterm delivery (4.27%), GDM, hypothyroid, Rh negative pregnancy (2.56% each), and cardiac disease and epilepsy (0.85% each).

Table 9. Maternal, clinical and ultrasound characteristics of the study population

Variables	Mean		Median	Range	
	Mean	SD		Min	Max
Age (Years)	24.41	4.00	24.00	19.00	36.00
Height (cms)	160.21	4.60	160.00	147.00	168.00
Weight (Kg)	55.03	4.68	55.00	25.00	65.00
Body mass index (Kg/m ²)	21.91	1.66	21.00	20.00	28.00
S/D ratio	2.87	0.81	3.00	1.00	5.00
RI	1.04	0.30	1.00	0.00	2.00
PI	1.67	0.62	1.65	0.21	3.00
Birth weight (kg)	2.69	0.55	2.80	0.10	4.40
Period of gestation (weeks)	37.82	3.16	38.29	21.29	40.86

The Maternal, clinical and ultrasound characteristics of the study population are as shown in the Table 13.

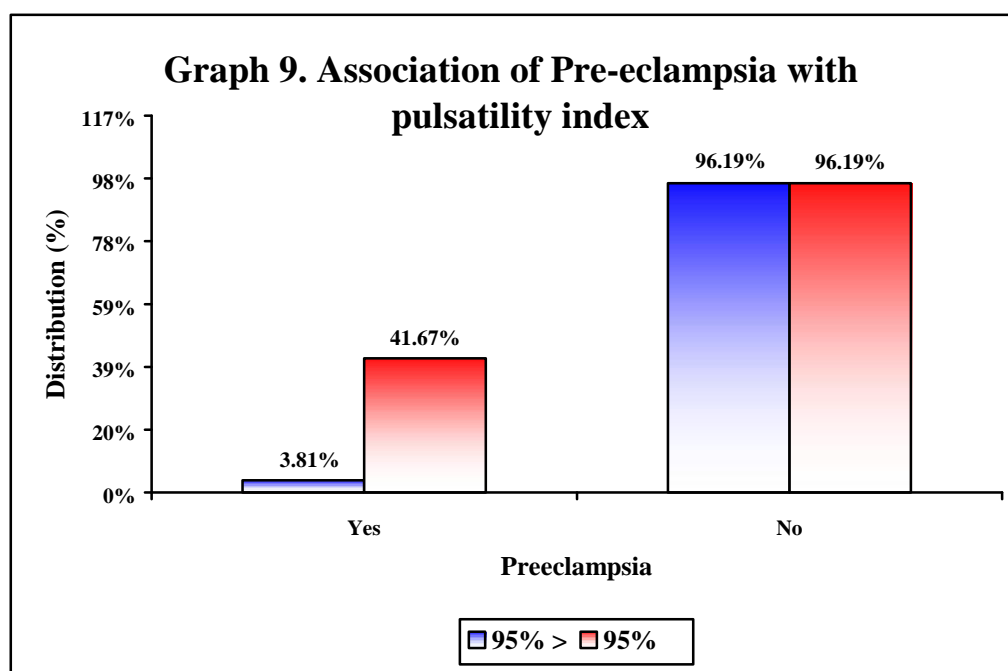
Table 10. Association of preeclampsia with pulsatility index

Pulsatility index (%)	Preeclampsia				Total (n=100)	
	Yes		No		No	%
	No	%	No	%		
95	5	41.67	7	58.33	12	100.00
< 95	4	3.81	101	96.19	105	100.00
Total	9	7.69	108	92.31	117	100.00

$$x^2=21.736$$

$$p= <0.001$$

Sensitivity=55.56%; specificity=93.52%; PPV=41.67%; NPV=96.19% Positive likelihood ratio=8.57; negative likelihood ratio=0.48 Kappa Agreement= 0.426 (0.146 to 0.705)



In the present study significantly higher number of women with pulsatility index 95% had preeclampsia (41.67% vs 3.81%; $p<0.001$). The sensitivity of PI in prediction of preeclampsia was 55.56% with specificity of 93.52% and there was moderate agreement with Kappa value of 0.426 (95% CI 0.146 to 0.705)

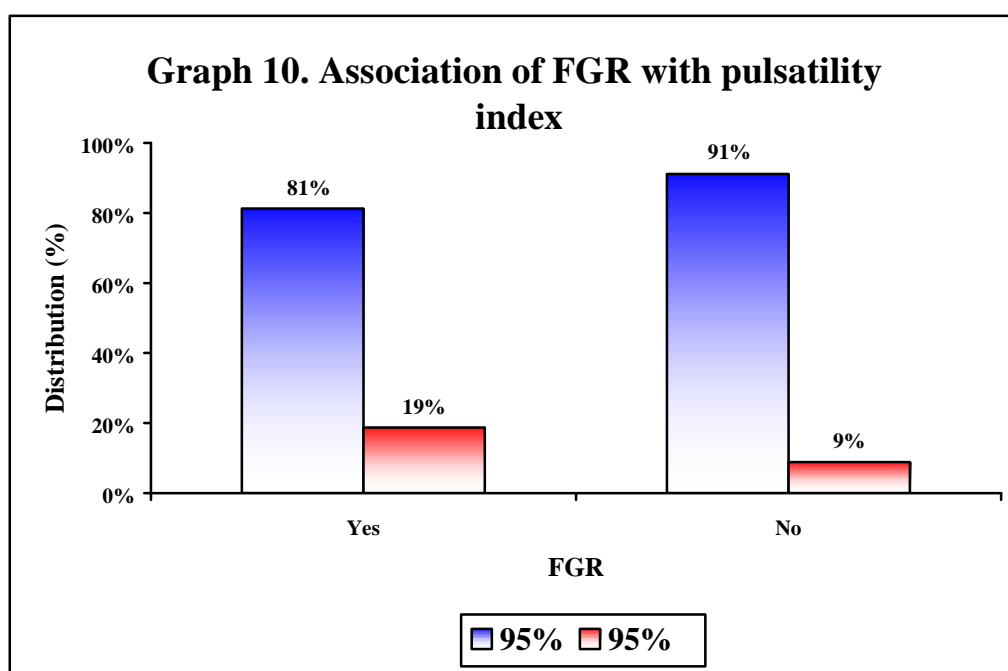
Table 11. Association of FGR with pulsatility index

Pulsatility index (%)	FGR				Total (n=100)	
	Yes		No		No	%
	No	%	No	%		
95	3	25.00	9	75.00	12	100.00
< 95	13	12.38	92	87.62	105	100.00
Total	16	13.68	101	86.32	117	100.00

$$x^2=1.453$$

$$p= 0.228$$

Sensitivity=18.75%; specificity=91.09%; PPV=25%; NPV=87.62% Positive likelihood ratio=2.10; negative likelihood ratio=0.89; Kappa Agreement= -0.110 (0.110 to 0.329)



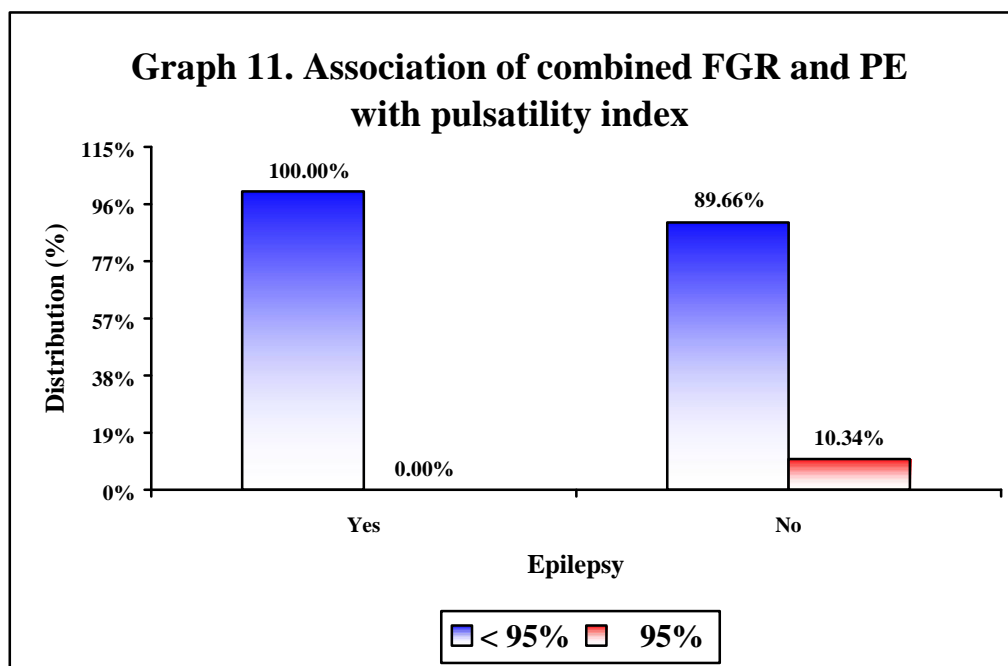
In the present study no association was found between pulsatility index and FGR ($p=0.228$). The sensitivity of PI in prediction of FGR was 18.75% with specificity of 91.09% and there was poor strength of agreement with Kappa value of -0.110 (95% CI 0.110 to 0.329).

Table 12. Association of combined FGR and PE with pulsatility index

FGR and PE	Pulsatility index (%)				Total (n=100)	
	< 95		95		No	%
	No	%	No	%		
Yes	2	50.00	2	50.00	4	100.00
No	103	91.15	10	8.85	113	100.00
Total	105	89.74	12	10.26	117	100.00

$\chi^2=7.107$

$p= 0.008$



In the present study significantly higher number of women (66.67%) with FGR and PE had pulsatility index >95%. (p=0.008).

Table 13. Distribution of women according to the gestational age at screening

Gestational age (weeks)	Distribution (n=117)	
	Number	Percentage
11 to 11+6	14	11.97
12 to 12+6	59	50.4
13 to 13+6	44	37.61
Total	117	100.00

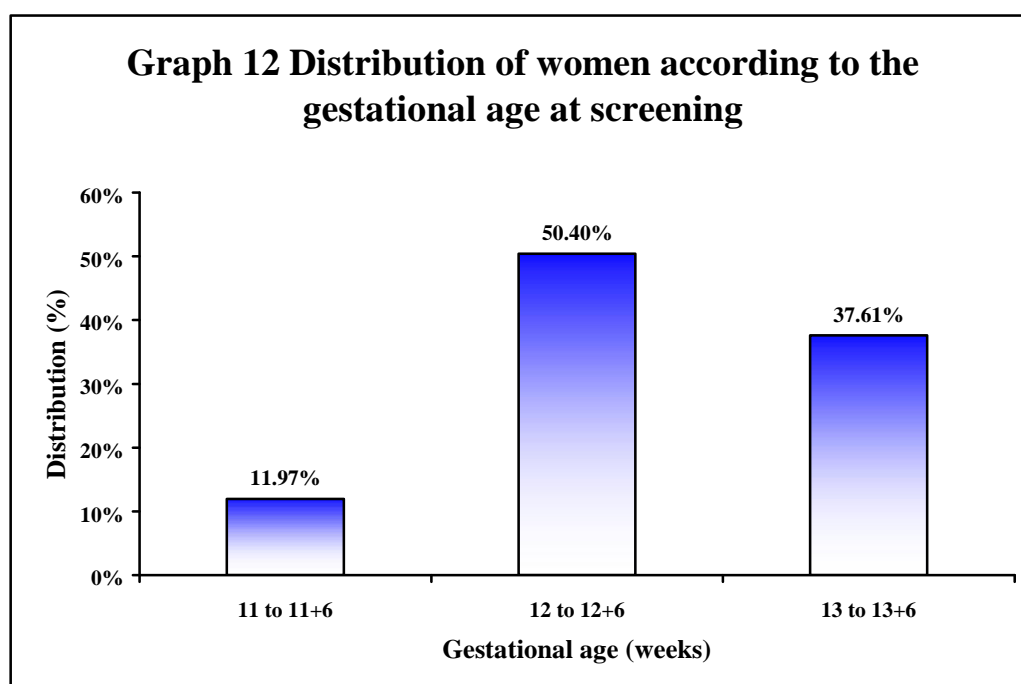
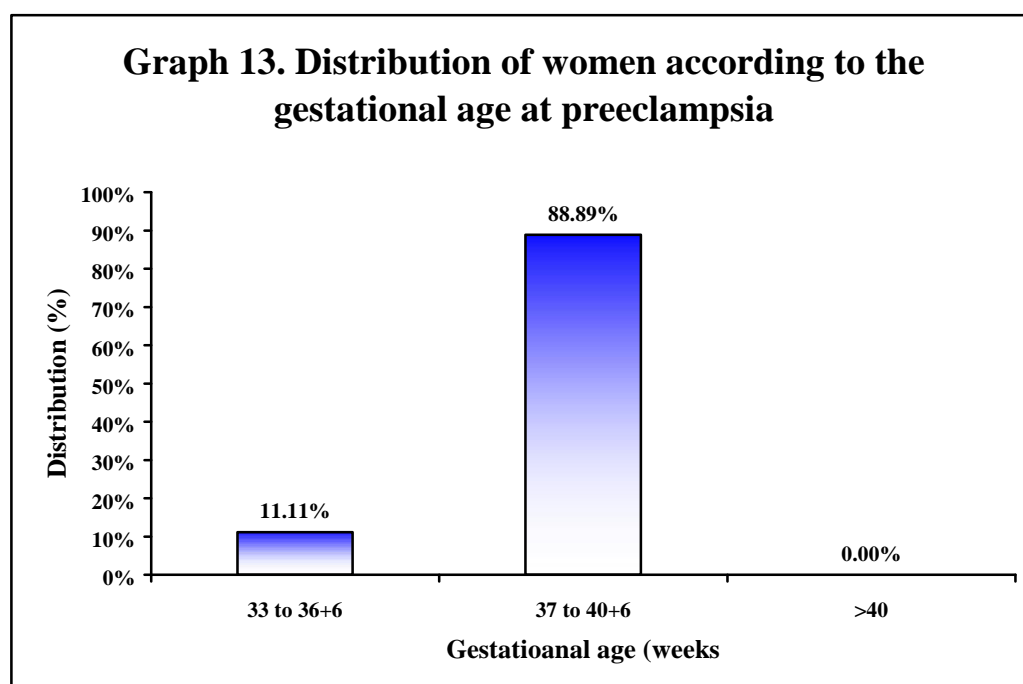


Table 14. Distribution of women according to the gestational age at which preeclampsia was detected

Gestational age (weeks)	Distribution (n=9)	
	Number	Percentage
33 to 36+6	1	11.11
37 to 40+6	8	88.89
> 40	0	0.00
Total	9	100.00



In this study most of the women underwent developed preeclampsia between 37 to 40+6 weeks of gestation. The mean gestational age at preeclampsia was 38.00 ± 2.12 weeks and median gestational age was 38 weeks (Range 33 to 40 weeks).

DISCUSSION

Uterine artery Doppler wave form analysis has been extensively studied in the second trimester of pregnancy as a predictive marker for the later development of preeclampsia and fetal growth restriction. The use of Doppler studies in the first trimester has gained momentum in recent years.^{68,84-90} This study was aimed to evaluate bilateral uterine artery Doppler between 11+0 to 13+6 weeks in the prediction of pregnancies that subsequently develop preeclampsia and IUGR.

The present study was done in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi. A total of 117 pregnant women with gestational age 11+0 to 13+6 weeks of gestation from January 2016 to February 2017 attending antenatal checkup were studied.

In the present study age ranged between 19 to 36 years. More than half of the study population that is, 50.43% of the women were aged between 21 to 25 year. The mean age was 24.41 ± 4 years suggesting that most of the women in our study were young. In contrast to these observations a large study by Gomez O et al.⁶⁸ in Spain reported mean maternal age as 30.5 years and age ranged between 14 to 44 years. The younger age of the women observed in the present study can be attributed to the early marriage practices in India.

With regard to obstetric history, most of the women were gravida 2 (44.44%) followed by gravida 1 (36.75%), gravida 3 (12.82%), gravida 4 (4.27%) and gravida 5 (1.71%). Majority of the women (97.44%) had BMI between 19.80 to 26.00 Kg/m². The mean BMI was 21.91 ± 1.6 Kg/m² and median BMI was noted as 21 Kg/m². The median BMI observed in the present study was comparable with a similar study by

Gomez et al.⁶⁸ who reported median BMI as 23.9 Kg/m² with range 16.3 being minimum and 70.5 Kg/m² being maximum.

In this study doppler assessment of uterine circulation for uterine artery indices was done using Voluson S8 ultrasound machine with 7.5 MHz transabdominal transducer. The pulsatility index ranged between 2% to 99 percentile. It was observed that, majority of the women (89.74%) had pulsatility index of <95% and 95 in 10.26% of the women. The mean pulsatility index was 54.96±28.75 percentile suggesting normal studies in most of the women.

In the present study the birth weight ranged between 0.1 to 4.40 Kgs and most of the babies that is, 47.01% of the babies had normal birth weight that is between 2.500 to 2.999 kg and 29.91% of the babies weighed between 3.000 to 3.499 Kg (29.91%). The mean birth weight was 2.69±0.55 Kgs. These finding suggest that most of the babies in this study had normal birth weight.

In this study gestational age at delivery ranged between 21.29 weeks to 40.86 weeks. However majority of the women (78.63%) delivered between 37 to 39+6 weeks. The mean gestational age at delivery was 37.82±0.55 weeks and the median gestational age at delivery was 38.29 weeks with range. These findings suggest that most of the women had term delivery. There were five preterm deliveries of them, one each (0.85%) had FSB, FSB with IUD, Severe FGR, IUD and PTD.

In this study out of 117 women, 30 (25.64%) women had comorbidities and the most common comorbidity was FGR noted in 16 (13.68%) women. The other uncommon comorbidities noted were preterm delivery (4.27%), GDM (2.56%), hypothyroid (2.56%), Rh negative pregnancy (2.56%), and very few that one women

each had cardiac disease (0.85%) and epilepsy (0.85%). Overall in this study not many women were identified to have a high proportion of severe complications.

The present study showed positive association between preeclampsia and pulsatility index as significantly higher number of women with pulsatility index of 95% had preeclampsia (55.56%) compared to only 3.81% of the women with pulsatility index <95%. This difference was statistically significant ($p < 0.001$). Further, the sensitivity of PI with a cut off value of 95% in prediction of preeclampsia was 55.56% with specificity of 93.52%, PPV of 41.67% and NPV of 96.19%. There was moderate agreement with Kappa value of 0.426 (95% CI 0.146 to 0.705). The Harrington et al.⁹¹ evaluated the abnormal uterine artery Dopplers at 12 to 16 weeks in 652 consecutive women the use of a seven parameter model which included uterine and umbilical artery Doppler parameters²² and found increased risk for preeclampsia and intrauterine growth retardation (IUGR). Harrington et al.⁹¹ examined 652 women at 12–16 weeks of gestation and reported a sensitivity of 93% and a specificity of 85% for the prediction of pre-eclampsia which was very high compared to the present study which showed sensitivity of 55.56% with specificity of 93.52%. This disagreement may be explained by the methodological differences and large sample size in the study by Harrington et al.⁹¹ Another study by Gomez O et al.⁶⁸ reported sensitivity of 24%, specificity of 95.1%, PPV of 11.3% and NPV of 97.9% in prediction of preeclampsia using a cut-off value of 95% PI which was in agreement with the present study.

In the present study the sensitivity of PI with a cut off value of 95% in prediction of preeclampsia was 55.56% with specificity of 93.52%, PPV of 41.67% and NPV of 96.19%. There was moderate agreement with Kappa value of

0.426 (95% CI 0.146 to 0.705). Poon et al.⁸⁶ investigated the role of uterine artery Doppler in the development of a predictive model for prediction of early preeclampsia. The detection rates for early preeclampsia, late preeclampsia, and gestational hypertension achieved by a model incorporating clinical history (history of preeclampsia, chronic hypertension, and method of conception) and maternal demographics (age, BMI, and ethnicity) alone were 47%, 41%, and 31%, respectively, at a 10% false positive rate.

The present study found statistically significant association with PI $\geq 95\%$ and preeclampsia ($p < 0.001$) which is in agreement with the study by Harrington et al.⁹¹ However, in contrast to the observations by Harrington et al.⁹¹ the present study showed no association was between pulsatility index and FGR ($p = 0.228$). The sensitivity of PI in prediction of FGR was low 18.75% with higher specificity of 91.09% and there was poor strength of agreement with (Kappa value of -0.110; 95% CI 0.110 to 0.329). Differences in demographic characteristics and in pregnancy outcomes between the two populations may explain this discrepancy. However, the sensitivity of pulsatility index with a cut-off value of $\geq 95\%$ in predicting FGR observed in this study was comparable with a study by Gomez O et al.⁶⁸ who reported sensitivity of 24.3%, specificity of 95.4%, PPV of 16.9% and NPV of 97% in prediction of FGR.

In the present study significantly higher number of women (66.67%) with FGR and PE had pulsatility index ≥ 95 ($p = 0.008$) suggesting positive association between $\geq 95\%$ PI and FGR in delivery complicated by PE.

In 2005, Gomez et al.⁶⁸ published a prospective trial PI greater than the 95th percentile was used as the cut-off value. The outcomes were preeclampsia and IUGR

but also gestational hypertension, abruption, and stillbirth. Unlike the study by Martin, they noted a progressive decline in the PI from 11 to 14 weeks and decreased rates of notching as gestation progressed.. Using the 95th percentile as a cut-off they could identify 24% of complicated pregnancies (preeclampsia and IUGR) and 31% of severe cases.

Overall to conclude though PI of 95% is associated with development of preeclampsia and FGR in pregnancy complicated by preeclampsia, it is not associated with development of FGR. The predictive accuracy of first-trimester uterine artery doppler showed low sensitivity (55.56%) with high specificity (93.52%) in predicting preeclampsia. Also the predictive accuracy of first-trimester uterine artery Doppler is low that is, sensitivity of 18.75% and high specificity of 91.09%. The low sensitivity of this test limits its utility as a disease marker in isolation.

However these findings need further validation due to certain limitations of this study. That is, smaller sample size and single center design. Which limit the observations from study in generalizing to the entire population. Hence 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.

There is growing evidence that multiparametric models in the first trimester have the potential to improve detection rates for preeclampsia and other adverse pregnancy outcomes. Algorithms that combine maternal characteristics, uterine artery Doppler velocimetry, and biochemical markers in the first trimester have the potential to improve the detection rate of early-onset preeclampsia to over 90% at a false positive rate of 10%.

CONCLUSION

The present study showed positive association between PI of $\geq 95\%$ with development of preeclampsia and FGR in pregnancy complicated by preeclampsia. However, PI of $\geq 95\%$ is not associated with development of FGR alone.

The predictive accuracy of first-trimester uterine artery doppler using PI with a cut off value of $\geq 95\%$ has low sensitivity in predicting preeclampsia (55.56% and IUGR (18.75%) with high specificity (93.52% and 91.09% respectively). Hence the low sensitivity of this test limits its utility as a disease marker in isolation.

Positive predictive value for prediction of PE and FGR of mean pulsatility index is low at 11-13⁶ weeks.

In view of high negative predictive value, this test would be better in screening a population at high risk.

Uterine artery Doppler screening should be combined with serum biochemical markers of platelet activation and endothelial damage to further improve the screening results.

SUMMARY

Uterine artery Doppler waveform analysis has been extensively studied in the second trimester of pregnancy as a predictive marker for the later development of preeclampsia and fetal growth restriction. The use of Doppler in the first trimester has gained momentum in recent years. Various measurement techniques and impedance indices have been used to evaluate the relationship between uterine artery Doppler velocimetry and adverse pregnancy outcomes. This study was evaluated bilateral uterine artery Doppler in pregnant women with gestational age between 11+0 to 13+6 weeks in the prediction of preeclampsia and IUGR.

The present one year longitudinal prospective cohort study conducted in the on 117 pregnant women with gestational age between 10+0 to 13+6 weeks attending antenatal checkup in the Department of Obstetrics and Gynecology, KLES Dr Prabhakar Kore Charitable Hospital and Medical Research Center, Belagavi from January 2016 to December 2016. the salient findings of the study are summarized as below.

- The most common age group was between 21 to 25 years (50.43%). The mean age was 24.41 ± 4 years.
- In this study most of the women were gravida 2 (44.44%)
- Majority (97.44%) of the women had BMI between 19.80 to 26.00 Kg/m^2 . The mean BMI delivery was 21.91 ± 1.6 Kg/m^2 .

- The pulsatility index ranged between 2% to 99%. Majority of the women (89.74%) had normal pulsatility index (<95%) and high (>95) in 10.26% of the women. The mean pulsatility index was 54.96 ± 28.75 percent.
- Labour was induced among 8.55% of the women and most common indication for the induction was PROM (40.00%).
- Most of the women (57.26%) had vaginal delivery and 42.74% underwent for LSCS. Most common indication for LSCS was Previous LSCS (38.00%) followed by fetal distress (32.00%).
- Most of the babies weighed between 2.500 to 2.999 kg (47.01%) and the mean birth weight was 2.69 ± 0.55 Kgs.
- Most of the women delivered between 37 to 39+6 weeks (78.63%). The mean gestational age at delivery was 37.82 ± 0.55 weeks.
- In this study out of 117 women, 30 (25.64%) women had comorbidities. Most common comorbidity was FGR (13.68%) followed by preeclampsia (7.69%). There were five preterm deliveries.
- Significantly higher number of women with pulsatility index >95% had preeclampsia (55.56%) ($p < 0.001$) and the sensitivity of PI in prediction of preeclampsia was 55.56% with specificity of 93.52% and there was moderate agreement with Kappa value of 0.426 (95% CI 0.146 to 0.705).
- No association was found between pulsatility index and FGR ($p = 0.228$). The sensitivity of PI in prediction of FGR was 18.75% with specificity of 91.09% and there was poor strength of agreement with Kappa value of -0.110 (95% CI

0.110 to 0.329) and). The sensitivity of PI in prediction of FGR was 18.75% with specificity of 91.09% and there was poor strength of agreement with Kappa value of -0.110 (95% CI 0.110 to 0.329).

- The present study showed positive association between PI of 95% with development FGR in pregnancy complicated by preeclampsia (p=0.008).
- No association was found between mode of delivery and pulsatility index (p=0.591) as well as between mode of delivery and FGR (p=0.527).

Based on the findings of this study it may be concluded that, PI of 95% is strongly associated with development of preeclampsia and FGR in pregnancy complicated by preeclampsia. However, PI of 95% is not associated with development of FGR alone and mode of delivery. The low sensitivity of PI limits its utility as a marker in isolation of the disease.

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ANNEXURE I – CONSENT FORM

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mrs. _____ we are requesting you to enroll yourself in study titled **“EVALUATION OF UTERINE ARTERY DOPPLER AT 11-13⁺⁶ WEEKS FOR PREDICTION OF PRE-ECLAMPSIA-A DESCRIPTIVE OBSERVATIONAL STUDY”** conducted by Dr. _____, Post Graduate in M.S. Obstetrics and Gynaecology under the guidance of Dr. _____, Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, under KLE University, Belagavi.

Respected Madam we request you to participate in our study. Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with Jawaharlal Nehru Medical College. If you decide to quit you are free to withdraw at any time.

The purpose of research is to assess whether early uterine artery Doppler at 11+0-13+6 weeks helps in prediction of pre-eclampsia.

Procedure Involved

If you agree to enroll yourself in my study, you will be interviewed regarding your present, past and family history, then you will be clinically examined in detail and investigated accordingly. A transabdominal ultrasound will be used for Doppler assessment of uterine artery indices at 11+0-13+6 weeks. You will be asked to follow up for ultrasound on specific dates given to you. You will be followed up to delivery to analyses outcome of your pregnancy.

Risk and Benefits

The benefits of taking part in this research is early diagnosis of pre-eclampsia by uterine artery Doppler at 11+0-13+6 weeks.

Voluntary Participation/Withdrawal

Taking part in the study is voluntary. You may choose not to enroll yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E. hospital.

Alternatives

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results

When the result of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Financial Incentives for participation

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Compensation

In the event of injury related to the study, treatment will be made available through KLES Hospital & MRC, Belagavi. There is no compensation or payment for such medical treatment by law.

Questions

In case you have any questions related to the study, in future or in case of study related injury or illness, you can contact Dr. _____, Department of Obstetrics and Gynaecology, KLES Hospital and MRC, Ph. No. _____ or phone number: _____ or Dr. _____, Professor, Department of Obstetrics and Gyanaecology, KLES Hospital and MRC, Belagavi Ph.: _____ or phone number: _____

If you have any queries about your rights as a study subject, you may call Dr. _____, Prof of PATHOLOGY as Chairman of Jawaharlal Nehru Medical College Institutional Ethics Committee on Human Subjects Research, Phone No. _____ at Jawaharlal Nehru Medical College, Belagavi or phone number: _____

Consent for participation ion research trial

I, _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read the literature in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name: _____

Signature or the Left Thumb Print of Subject: _____ Date: _____

Witness Name (1): _____ **Signature:** _____ **Date:** _____

Witness Name (1): _____ **Signature:** _____

Date: _____

Investigators Name: _____ Signature: _____

Date: _____

Place: _____

If the consenting woman is illiterate:

The woman will be asked to print her thumb under “Woman’s signature or thumb print” and print the Name of an Independent Literate Witness, the date and the signature of the Witness (if possible, this person should be selected by the participant and should have no connection to the research team) after the below statement:

I was present while the benefits, risk and procedures were read to the volunteer. All questions she had were answered and she has agreed to participate in the study.

Witness’s name: _____

Witness’s signature: _____

Date: _____

Signature of the Investigator: _____

ANNEXURE II – PROFORMA

**“PREDICTION OF PRE-ECLAMPSIA IN PREGNANCY-EVALUATION OF
UTERINE ARTERY DOPPLER AT 11+0 TO 13+6 WEEKS – ONE YEAR
PROSPECTIVE COHORT STUDY”**

Name: _____

Age: _____

Address: _____

Phone No: _____

Date of admission: _____

In patient number: _____

Menstrual History

LMP:

POG:

EDD:

USG EDD:

Obstetric History

Gravida

Para:

Living:

Abortion:

Dead:

Still birth:

Past History

History of diabetes: Yes/No

History of hypertension: Yes/No

History of Tuberculyasis: Yes/No

USG

First Trimester

Gestational Age:	
CRL:	
EDD:	
DOPPLER INDICES:	
S/D:	
RI:	
PI:	

GENERAL EXAMINATION:

Height:

Weight:

BMI:

Pedal edema:

Follow up:

PR:

BP:

Maternal outcome:

Route of delivery:

Vaginal

Caesarean section

Indication: _____

Complications: _____

Weeks	Onset of PE	Detection of FGR	GA at delivery
<28			
28-34			
34-37			
>37			

Neonatal outcome:

Birth weight:

Sex:

Apgar score:

Date:

ANNEXURE 3 – ETHICAL CLEARANCE



K.L.E.UNIVERSITY'S

JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
(Accredited 'A' Grade by NAAC)

Website: <http://www.jnmc.edu>
E-Mail : dome@jnmc.edu

Phone: (+ 91-(0)831 Office : 2471350
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 391

Date: 18/11/2015

To,

REG NO.BJ0115005

PG student in OBG,
J.N.Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled "PREDICTION OF PRE-ECLAMPSIA IN PREGNANCY – EVALUATION OF UTERINE ARTERY DOPPLER AT 11+0 TO 13+6 WEEKS AT KLES PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE, BELGAUM. ONE YEAR PROSPECTIVE COHORT STUDY", is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Arathi Darshan)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Ganga Pilli)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE III – KEY TO MASTER CHART

-	-	Absent
cm	-	Centimeter
CRL	-	Crown rump length
EDD	-	Estimated date of delivery
FGR	-	Fetal growth restriction
FSB	-	Fetal stillbirth
FTD	-	Fullterm delivery
IUD	-	Intrauterine death
Kg	-	Kilogram
Kg/m ²	-	Kilogram per square meter
LSCS	-	Lower segment caesarean section
ND	-	Normal delivery
PI	-	Pulsatility index
POG	-	Period of gestation
PPROM	-	Preterm premature rupture of membrane
PROM	-	Premature rupture of membrane
PTD	-	Preterm delivery
RI	-	Resistance index
Sev oligo	-	Severe oligohydramnios
wk	-	weeks

Chapter 1

Introduction



Chapter 2

Objectives



Chapter 3

Review of Literature



Chapter 4

Methodology



Chapter 5

Results



Chapter 6

Discussion



Chapter 7

Conclusion



Chapter 8

Summary



Chapter 9

Bibliography



Chapter 10

Annexures



Master Chart

Serial number	In patient number	Age (YEARS)	Age (YEARS)	Date of admission	History											Physical examination				
					Menstrual history			Obetric history					Past history			Height (cm)	Weight (Kg)	BMI (Kg/m2)	Gestational age	
					LMP		USG EDD	Gravida	Para	Living	Abortion	Dead	Still birth	Diabetes mellitus	Hypertension					Tuberculosis
					POG	EDD														
1		24	21 to 25	12/1/2015	13	6/5/2016		1						no	no	no	152	58	25	13
2		25	21 to 25	12/1/2015	12	6/4/2016		3	1	1	1			no	no	no	160	54	21	12
3		20	19 to 20	12/4/2015	13	6/9/2016		2	1	0		1		no	no	no	154	50	22	13
4		30	26 to 30	12/4/2015	13	6/9/2016		3	1	1	1			no	no	no	158	58	24	13
5		24	21 to 25	12/5/2015	12	6/13/2016		3	1	1	1			no	no	no	164	65	25	12
6		20	19 to 20	12/8/2015	13	6/21/2016		2	1	1				no	no	no	156	54	22	13
7		19	19 to 20	12/8/2015	12	6/16/2016		1						no	no	no	158	52	21	12
8		20	19 to 20	12/15/2015	12	6/27/2016		1						no	no	no	160	58	23	12
9		22	21 to 25	12/15/2015	12	6/27/2016		1						no	no	no	160	54	21	12
10		24	21 to 25	12/22/2015	12	6/13/2016		3	1	1	1			no	no	no	158	50	20	12
11		23	21 to 25	12/22/2015	12	7/1/2016		2	1	1				no	no	no	156	48	20	12
12		25	21 to 25	12/22/2015	13	6/24/2016		2	1	1				no	no	no	158	52	21	13
13		19	19 to 20	1/4/2016	13	7/9/2016		1						no	no	no	162	54	20	13
14		26	26 to 30	1/9/2016	12	7/22/2016		2	1	1				no	no	no	163	52	20	12
15		23	21 to 25	1/16/2016	12	7/4/2016		2	1	1				no	no	no	164	55	21	12
16		20	19 to 20	1/20/2016	12	7/30/2016		3	2	2				no	no	no	162	53	20	12
17		19	19 to 20	1/23/2016	13	7/28/2016		2	1	1				no	no	no	160	52	21	13
18		24	21 to 25	1/23/2016	13	7/18/2016		1						no	no	no	164	55	21	13
19		27	26 to 30	2/1/2016	13	8/4/2016		3	1		1			no	no	no	162	50	20	13
20		25	21 to 25	3/11/2016	13	10/2/2016		2			1			no	no	no	158	50	20	13
21		22	21 to 25	3/11/2016	13	9/17/2016		1						no	no	no	162	56	22	12
22		21	21 to 25	3/15/2016	12	9/12/2016		2		1				no	no	no	162	54	22	12
23		27	26 to 30	3/15/2016	11	9/30/2016		2		1				no	no	no	166	58	23	11
24		31	31 to 35	3/15/2016	12	9/22/2016		2	1	1				no	no	no	160	52	21	12
25		35	31 to 35	3/15/2016	13	9/24/2016		2	1	1				no	no	no	166	55	22	12
26		26	26 to 30	3/21/2016	12	9/29/2016		5	2	2	1			no	no	no	164	57	22	12
27		22	21 to 25	3/25/2016	12	9/28/2016		2	1	1				no	no	no	158	54	21	12
28		27	26 to 30	3/28/2016	12	10/3/2016		1						no	no	no	168	60	21	12
29		22	21 to 25	3/28/2016	13	9/29/2016		1						no	no	no	164	56	21	13
30		25	21 to 25	3/29/2016	13	10/3/2016		2	1	1				no	no	no	162	54	20	13
31		24	21 to 25	3/29/2016	12	9/28/2016		1						no	no	no	166	58	23	12
32		20	19 to 20	4/1/2016	12	#####		1						no	no	no	158	52	21	12
33		25	21 to 25	4/5/2016	12	#####		3	2	2				no	no	no	160	52	21	12
34		25	21 to 25	4/5/2016	11	#####		2	1	1				no	no	no	162	58	23	11
35		29	26 to 30	4/4/2016	12	#####		3	2	2				no	no	no	166	54	22	12
36		25	21 to 25	4/18/2016	13	#####		1						no	no	no	164	56	21	13
37		25	21 to 25	4/19/2016	12	#####		2	1	1				no	no	no	162	60	22	12
38		20	19 to 20	4/19/2016	12	#####		2			1			no	no	no	158	54	21	12
39		35	31 to 35	4/25/2016	12	11/2/2016		3	1	1	1			no	no	no	164	56	21	12
40		22	21 to 25	4/30/2016	12	11/9/2016		4			3			no	no	no	158	54	21	12
41		23	21 to 25	4/30/2016	12	#####		4	1	1	2			no	no	no	158	52	21	12
42		27	26 to 30	5/2/2016	13	#####		1						no	no	no	155	50	22	13

43	22	21 to 25	5/2/2016	12	#####	2			1			no	no	no	164	58	22	12
44	21	21 to 25	5/7/2016	13	11/8/2016	2	1	1				no	no	no	160	54	21	13
45	19	19 to 20	5/7/2016	12	#####	1						no	no	no	162	54	20	12
46	22	21 to 25	5/7/2016	13	#####	1						no	no	no	165	62	21	13
47	21	21 to 25	5/16/2016	12	#####	2			1			no	no	no	160	52	21	12
48	20	19 to 20	5/16/2016	13	#####	1						no	no	no	156	48	20	13
49	28	26 to 30	5/16/2016	12	#####	1						no	no	no	164	60	20	12
50	29	26 to 30	5/17/2016	12	#####	4	2	1	1			no	no	no	162	54	20	12
51	27	26 to 30	5/20/2016	12	#####	2	1	1				no	no	no	166	58	23	12
52	34	31 to 35	5/20/2016	13	#####	2	1	1				no	no	no	164	55	21	13
53	20	19 to 20	5/20/2016	11	#####	1						no	no	no	158	52	21	11
54	20	19 to 20	5/20/2016	11	#####	1						no	no	no	154	56	23	11
55	19	19 to 20	5/23/2016	12	#####	2	1	1				no	no	no	160	52	20	13
56	24	21 to 25	5/23/2016	12	12/4/2016	2	1	1				no	no	no	164	55	20	12
57	19	19 to 20	5/23/2016	14	#####	2			1			no	no	no	166	54	21	12
58	34	31 to 35	5/23/2016	13	#####	1						no	no	no	168	64	23	12
59	29	26 to 30	5/30/2016	12	#####	2	1	1				no	no	no	162	54	22	12
60	22	21 to 25	5/30/2016	12	12/7/2016	2	1					no	no	no	160	52	21	12
61	21	21 to 25	6/1/2016	13	12/2/2017	2	1	1				no	no	no	162	52	22	13
62	27	26 to 30	6/6/2016	12	#####	2	1	1				no	no	no	166	57	22	12
63	22	21 to 25	6/6/2016	12	#####	2	1	1				no	no	no	168	64	23	12
64	27	26 to 30	6/6/2016	13	12/8/2016	1						no	no	no	165	62	21	13
65	21	21 to 25	6/13/2016	13	#####	2			1			no	no	no	164	55	21	13
66	24	21 to 25	6/13/2016	12	#####	1						no	no	no	166	65	25	12
67	20	19 to 20	6/13/2016	12	#####	2			1			no	no	no	156	58	21	12
68	23	21 to 25	6/14/2016	13	#####	3	1	1	1			no	no	no	162	55	22	13
69	23	21 to 25	6/17/2016	13	#####	1						no	no	no	155	52	21	13
70	26	26 to 30	6/17/2016	13	#####	1						no	no	no	160	55	22	13
71	31	31 to 35	6/27/2016	12	1/6/2017	2			1			no	no	no	164	54	21	12
72	22	21 to 25	6/28/2016	13	1/1/2017	1						no	no	no	160	52	21	13
73	24	21 to 25	7/4/2016	14	#####	3	1	1	1			no	no	no	162	58	22	12
74	24	21 to 25	8/1/2016	12	2/13/2017	1						no	no	no	156	60	23	12
75	20	19 to 20	8/1/2016	13	2/4/2017	1						no	no	no	154	56	23	13
76	23	21 to 25	8/1/2016	13	1/7/2017	1						no	no	no	164	55	21	13
77	20	19 to 20	8/1/2016	13	2/2/2017	1						no	no	no	160	52	22	13
78	35	31 to 35	8/5/2016	11	2/13/2017	2	1	1				no	no	no	160	55	22	12
79	22	21 to 25	8/8/2016	12	2/19/2017	1						no	no	no	158	52	20	12
80	19	19 to 20	8/8/2016	13	2/6/2017	1						no	no	no	158	52	21	13
81	28	26 to 30	8/8/2016	12	2/13/2017	1						no	no	no	156	58	21	12
82	22	21 to 25	8/22/2016	13	2/25/2017	2			1			no	no	no	160	52	21	13
83	23	21 to 25	8/22/2016	19	1/16/2017	1						no	no	no	162	55	22	13
84	21	21 to 25	8/26/2016	13	3/2/2017	1						no	no	no	166	60	23	13
85	21	21 to 25	8/29/2016	13	2/28/2017	1						no	no	no	152	58	25	13
86	22	21 to 25	9/2/2016	12	3/14/2017	2	1	1				no	no	no	158	61	24	12
87	21	21 to 25	9/2/2016	8	4/9/2017	1						no	no	no	162	57	21	11
88	24	21 to 25	9/12/2016	14	3/9/2017	2	1	1				no	no	no	156	54	22	11
89	27	26 to 30	9/12/2016	13	3/16/2017	1						no	no	no	160	54	23	12
90	30	26 to 30	9/17/2016	12	4/1/2017	2	1	1				no	no	no	160	55	22	12
91	25	21 to 25	9/19/2016	11	4/10/2017	1						no	no	no	147	50	23	11
92	24	21 to 25	9/19/2016	11	4/4/2017	1						no	no	no	160	50	20	11
93	28	26 to 30	9/23/2016	11	4/10/2017	4	2	2	1			no	no	no	164	65	24	11
94	26	26 to 30	9/23/2016	12	4/2/2017	2	1	1				no	no	no	156	25	22	11

95	25	21 to 25	9/26/2016	12	4/9/2017	3	1	1	1			no	no	no	167	60	23	12
96	24	21 to 25	9/26/2016	13	3/31/2017	2	1	1				no	no	no	154	56	23	13
97	32	31 to 35	10/8/2016	11	4/23/2017	3	2	1	1			no	no	no	165	55	21	11
98	29	26 to 30	10/27/2016	13	5/4/2017	2	1	1				no	no	no	160	52	20	13
99	28	26 to 30	11/12/2016	12	5/21/2017	1						no	no	no	158	56	22	12
100	28	26 to 30	11/17/2016	12	5/29/2017	4	2	1	1	1		no	no	no	165	62	23	12
101	21	21 to 25	11/17/2016	12	5/30/2017	2	1	1				no	no	no	164	58	22	12
102	26	26 to 30	11/17/2016	13	5/25/2017	2	1	1				no	no	no	166	62	23	13
103	24	21 to 25	11/23/2016	13	5/26/2017	5	3	1	1		2	no	no	no	168	62	21	13
104	23	21 to 25	12/1/2016	12	6/12/2017	2	1				1	no	no	no	158	62	24	12
105	27	26 to 30	12/15/2016	12	6/8/2017	2	1	1				no	no	no	158	52	20	12
106	22	21 to 25	12/15/2016	12	6/4/2017	2	1	1				no	no	no	160	50	20	12
107	26	26 to 30	1/6/2017	11	7/14/2017	1						no	no	no	158	56	22	11
108	28	26 to 30	1/6/2017	13	7/13/2017	1						no	no	no	148	55	25	13
109	21	21 to 25	1/6/2017	13	7/11/2017	1						no	no	no	150	55	25	13
110	27	26 to 30	1/7/2017	13	7/15/2017	2				1		no	no	no	147	50	23	13
111	24	21 to 25	1/9/2017	11	7/30/2017	2	1	1				no	no	no	152	55	23	11
112	21	21 to 25	1/19/2017	11	8/5/2017	2	1	1				no	no	no	156	52	21	11
113	24	21 to 25	1/20/2017	12	8/3/2017	3	2	1				no	no	no	154	56	23	12
114	20	19 to 20	1/20/2017	12	8/3/2017	2	1	1				no	no	no	148	54	25	12
115	32	31 to 35	1/23/2017	11	8/2/2017	3	2	2				no	no	no	160	55	22	11
116	36	> 35	1/23/2017	12	8/10/2017	2	1	1				no	no	no	160	52	20	12
117	25	21 to 25	2/2/2017	11	8/18/2017	2	1	1				no	no	no	162	57	21	11

USG Findings						Pre-eclampsia	Induction	Indication for induction	birth weight (Kg)	Mode of delivery	Indication for LSCS	PTD	POG (Weeks)	POG (Days)	POG	IUGR	GDM	Hypothyroid	Cardiac disease
First trimester																			
CRL	EDD	Doppler indices	S/D	RI	PI														
61	6/5/2016		4	1	90%	N	no	no	3.4	LSCS	FD	-	37	0	37	N	N	N	N
57	6/4/2016		3	1	60%	N	N	N	2.8	VD		-	38	0	38.00	N	N	N	N
76	6/8/2016		4	1	15%	N	N	N	4.4	LSCS	FD	-	37	0	37.00	N			
77	6/9/2016		2	1	30%	N	N	N	2.2	LSCS	rev lsc	-	39	0	39.00	Y			
59	6/13/2017		4	1	95%	Y	N	N	1.8	VD		-	38	2	38.29	Y			
72	6/13/2016		2	0	95%	Y	N	N	3.2	LSCS	clamps	-	40	3	40.43	N			
59	6/16/2016		4	1	50%	N	N	N	2.5	VD		-	37	0	37.00	N			
51	6/27/2016		4	1	30%	N	N	N	2.6	VD		-	38	4	38.57	N	N	N	N
62	6/27/2016		3	1	99%	Y	N	N	3.2	VD		-	39	5	39.71	N			
55	6/13/2016		4	1	30%	N	N	N	3	LSCS	FD	-	38	5	38.71	N			
54	7/1/2016		3	1	16%	N	N	N	2.5	LSCS	rev lsc	-	37	0	37.00	N			
75	6/24/2016		5	1	70%	N	N	N	3.1	VD		-	37	4	37.57	N	N	N	N
62	7/9/2016		4	1	38%	N	N	N	2.1	VD		-	38	0	38.00	Y	N	N	N
57	7/22/2016		3	0	52%	N	N	N	2.5	LSCS	FD	-	39	0	39.00	N	N	N	N
63	7/4/2016		3	1	8%	N	N	N	3	VD		-	38	1	38.14	N	N	N	N
67	7/30/2016		3	1	12%	N	N	N	3	VD		-	38	5	38.71	N	N	N	N
64	7/28/2016		4	1	40%	N	N	N	2.19	LSCS	rev lsc	-	38	2	38.29	Y	N	N	N
73	7/18/2016		4	1	85%	N	N	N	3	VD		-	39	0	39.00	N	N	Y	N
85	8/4/2016		4	1	3%	N	N	N	2.9	VD		-	38	6	38.86	N	N	N	N
68	10/2/2016		3	1	40%	N	N	N	2.8	VD		-	38	4	38.57	N	N	N	N
77	9/12/2016		3	1	50%	N	Y	PROM	2.9	VD		-	39	0	39.00	N	N	N	N
63	9/12/2016		3	1	62%	N	N	N	2.6	VD		-	39	0	39.00	N	N	N	N
48	9/30/2016		3	1	58%	N	N	N	2.3	LSCS	rev lsc	-	38	1	38.14	Y	N	N	N
67	9/22/2016		4	1	71%	N	N	N	2.3	LSCS	FD	-	36	2	36.29	N	N	N	N
74	9/18/2016		3	1	69%	N	N	N	2.8	LSCS	rev lsc	-	37	5	37.71	N	N	N	N
56	9/29/2016		3	1	61%	N	N	N	2.5	VD		-	36	2	36.29	N	N	N	N
60	9/28/2017		3	1	14%	N	N	N	3.1	VD		-	40	2	40.29	N	N	N	N
55	10/3/2016		4	1	61%	N	N	N	0.5	VD		PTD	21	2	21.29	N	N	N	N
72	9/29/2016		3	1	55%	N	N	N	3	LSCS	NPL	-	37	4	37.57	N	N	N	N
68	10/3/2016		4	1	50%	Y	N	N	3	LSCS	rev lsc	-	38	4	38.57	N	N	N	N
55	9/28/2016		3	1	14%	N	N	N	2.8	VD		-	37	0	37.00	N	N	N	N
61	10/10/2016		2	1	30%	N	N	N	2.9	VD		-	38	0	38.00	N	N	N	N
59	10/17/2016		3	1	69%	N	N	N	3.2	VD		-	38	4	38.57	N	N	N	N
54	10/20/2016		3	1	90%	N	N	N	2.5	LSCS	rev lsc	-	39	0	39.00	Y	N	N	N
58	10/16/2016		4	1	80%	N	N	N	3	LSCS	V 2 LS	-	38	0	38.00	N	N	N	N
69	10/20/2016		4	1	18%	N	N	N	2.8	LSCS	FD	-	40	2	40.29	N	N	N	N
61	10/28/2016		3	1	50%	N	N	N	3	LSCS	rev lsc	-	38	0	38.00	N	N	N	N
49	11/1/2016		3	1	60%	N	N	N	3.2	VD		-	38	0	38.00	N	N	N	N
61	11/2/2016		4	1	66%	N	N	N	2.9	LSCS	FD	-	39	0	39.00	N	N	N	N
52	11/9/2016		3	1	56%	N	N	N	2.6	VD		-	40	0	40.00	N	N	N	N
52	11/10/2016		3	1	60%	N	N	N	2.8	VD		-	39	0	39.00	N	N	N	N
67	11/5/2016		4	2	50%	N	N	N	2.4	VD		-	37	0	37.00	Y	N	N	N

54	11/12/2016		3	1	38%	N	N	N	2.5	VD		-	39	2	39.29	N	N	N	N
67	11/8/2016		2	1	12%	Y	N	N	3.3	LSCS	rev lsc	-	40	3	40.43	N	N	N	N
67	11/16/2016		3	1	99%	N	N	N	3.3	LSCS	FD	-	40	4	40.57	N	N	N	N
59	11/11/2016		4	1	99%	N	N	N	3.2	LSCS	FD	-	38	2	38.29	N	N	N	N
65	11/22/2016		3	1	3%	N	N	N	2.6	VD		-	40	4	40.57	N	N	N	N
70	11/19/2016		4	2	65%	N	N	N	2.9	VD		-	38	4	38.57	N	N	N	N
64	11/18/2016		3	2	50%	N	N	N	2.6	LSCS	NPL	-	37	0	37.00	N	N	N	N
61	11/13/2016		4	1	44%	N	N	N	0.89	VD		FSB	25	4	25.57	N	N	N	N
58	11/30/2016		3	1	50%	N	N	N	2.7	VD		-	38	6	38.86	N	N	N	N
73	11/25/2016		3	2	21%	N	N	N	2.6	LSCS	rev lsc	-	39	0	39.00	N			
43	11/30/2016		3	1	4%	N	N	N	3.1	LSCS	FD	-	39	2	39.29	N			
43	11/30/2016		3	1	90%	N	N	N	3	LSCS	NPL	-	39	0	39.00	N			
63	11/27/2016		4	1	83%	N	N	N	2.8	VD		-	37	0	37.00	N			
52	12/4/2016		3	2	80%	N	N	N	2.4	VD		-	39	3	39.43	Y			
63	11/29/2016		3	1	70%	N	N	N	2.3	VD		-	38	1	38.14	N			
65	12/1/2016		3	1	83%	N	Y	HNE	2.9	VD		-	40	0	40.00	N			
59	12/12/2016		4	1	60%	N	N	N	3.1	LSCS	rev lsc	-	37	2	37.29	N			
66	12/7/2016		3	1	55%	N	N	N	1.9	LSCS	rev lsc	-	32	0	32.00	N			
68	12/2/2017		3	1	48%	Y	N	N	1.2	VD		PTD(IUD)	33	0	33.00	Y	N	N	N
62	12/14/2016		3	1	59%	N	N	N	2.4	VD		-	39	0	39.00	Y	N	N	N
59	12/18/2016		4	2	4%	N	N	N	2.8	VD		-	40	5	40.71	N	N	N	N
62	12/8/2016		3	1	40%	N	N	N	2.6	LSCS	CPD	-	38	4	38.57	N	Y	N	N
64	12/14/2016		3	2	55%	N	N	N	3	LSCS	FD	-	40	3	40.43	N	N	N	N
51	12/26/2016		3	1	99%	N	Y	TDAT	3.3	VD		-	41	0	38.00	N	N	N	N
66	12/23/2016		3	1	5%	N	N	N	2.7	LSCS	FD	-	39	5	39.71	N	N	N	N
72	12/19/2016		3	1	70%	N	N	N	2.8	LSCS	rev lsc	-	37	4	37.57	N			
78	12/20/2016		3	2	45%	N	Y	PROM	2.4	VD		-	39	5	39.71	N	N	N	N
79	12/20/2016		4	1	8%	N	Y	PROM	2.7	VD		-	39	2	39.29	N	N	N	N
58	1/6/2017		3	1	99%	N	N	N	2.7	LSCS	CPD	-	37	4	37.57	N	N	Y	N
73	1/1/2017		3	1	4%	N	N	N	2.5	VD		-	38	0	38.00	N	N	N	N
60	1/10/2017		3	1	66%	N	N	N	2.4	VD		-	39	5	39.71	Y	N	N	N
56	2/13/2017		3	1	45%	N	N	N	3	VD		-	37	4	37.57	N	N	N	N
76	2/6/2017		3	1	95%	N	N	N	2.4	LSCS	FD	-	38	0	38.00	Y	N	N	N
62	1/7/2017		2	1	87%	N	N	N	2.8	LSCS	V 2 LS	-	39	0	39.00	N	N	N	N
62	2/2/2017		3	0	80%	N	N	N	2.6	LSCS	CPD	-	38	1	38.14	N	N	N	N
55	2/19/2017		2	1	23%	N	N	N	2.8	VD		-	39	5	39.71	N	N	N	N
62	2/19/2017		2	1	10%	N	N	N	3	VD		-	40	2	40.29	N	N	N	N
74	2/6/2017		2	1	35%	N	Y	IUD	1.4	VD		FSB+IUD	22	0	22.00	N	N	N	N
62	2/17/2017		2	1	75%	N	N	N	3.2	LSCS	LIQUE	-	38	5	38.71	N	N	N	N
53	3/3/2017		2	1	68%	N	N	N	0.1	VD	NCEP	PTD	16		23.00	N	N	N	N
78	2/24/2017		2	1	80%	N	N	N	2.4	ND		-	37	0	37.00	N	N	N	N
52	3/10/2017		2	1	95%	N	N	N	2.5	VD		-	37	5	37.71	N	N	N	N
75	2/28/2017		2	1	87%	Y	Y	PE	2.4	LSCS	FI	-	39	6	39.86	Y	N	N	N
54	3/14/2017		2	1	32%	N	N	N	2.7	VD		-	38	0	38.00	N	N	N	N
49	3/18/2017		2	1	60%	N	N	N	2.5	VD		-	37	2	37.29	N	N	N	N
49	3/28/2017		2	1	84%	N	N	N	3.01	LSCS	rev lsc	-	38	2	38.29	N	N	N	N
61	3/22/2017		2	1	53%	N	N	N	2.6	VD		-	38	6	38.86	N	N	N	N
53	4/1/2017		2	1	60%	N	N	N	2.8	VD		-	38	0	38.00	N	N	N	N
44	4/4/2017		3	1	56%	N	N	N	2.9	LSCS	CPD	-	39	0	39.00	N	N	N	N
44	4/4/2017		2	1	3%	N	N	N	2.6	LSCS	APH	-	37	2	37.29	N	N	N	N
54	4/10/2017		2	1	93%	N	N	N	2.7	VD		-	38	5	38.71	N	N	N	N
49	4/8/2017		3	1	2%	N	N	N	2.6	LSCS	FD	-	40	0	40.00	N	N	N	N

61	4/7/2017		2	1	63%	N	N	N	2.8	VD		-	37	4	37.57	N	N	N	N
78	3/31/2017		2	1	32%	N	N	N	3.6	LSCS	rev lsc	-	38	2	38.29	N	N	N	N
53	4/23/2017		3	1	74%	N	N	N	2.8	VD		-	39	0	39.00	N	N	N	N
61	5/4/2017		3	1	72%	N	N	N	2.9	LSCS	rev lsc	-	38	2	38.29	N	N	N	N
66	5/21/2017		2	1	68%	N	N	N	3	VD		-	37	4	37.57	N	N	N	Y
57	5/29/2017		2	1	50%	N	N	N	2.8	LSCS	rev lsc	-	37	0	37.00	N	Y	N	N
63	5/30/2017		2	1	92%	N	N	N	2.4	VD		-	40	4	40.57	Y	N	N	N
76	5/25/2017		3	1	51%	N	N	N	3.1	VD		-	40	0	40.00	N	N	N	N
77	5/26/2017		3	1	80%	N	N	N	3	VD		-	38	0	38.00	N	N	N	N
57	6/12/2017		2	1	60%	N	N	N	2.9	LSCS	NPL	-	37	2	37.29	N	Y	N	N
63	6/12/2017		1	1	70%	N	N	N	3	LSCS	rev lsc	-	37	6	37.86	N	N	N	N
59	6/12/2017		3	1	63%	N	N	N	2.8	VD		-	38	0	38.00	N	N	Y	N
55	7/27/2017		2	1	62%	N	N	N	3	LSCS	CPD	-	39	2	39.29	N	N	N	N
76	7/13/2017		2	1	4%	N	N	N	2.2	LSCS	FD	-	39	3	39.43	Y	N	N	N
77	7/11/2017		1	1	99%	Y	Y	PE	2.1	LSCS	FD	-	37	2	37.29	Y	N	N	N
76	7/15/2017		1	1	99%	Y	N	N	3.1	VD		-	38	0	38.00	N	N	N	N
45	7/30/2017		2	1	80%	N	Y	DATA	3.1	VD		-	41	6	40.86	N	N	N	N
44	8/5/2017		2	1	7%	N	N	N	1.9	LSCS	rev lsc	-	32	4	32.57	N	N	N	N
62	8/3/2017		1	1	29%	N	N	N	2.9	VD		-	38	0	38.00	N	N	N	N
62	8/3/2017		2	1	99%	N	N	N	3.4	VD		-	38	0	38.00	N	N	N	N
46	8/2/2017		2	1	34%	N	N	N	2.7	VD		-	37	5	37.71	N	N	N	N
44	8/10/2017		2	1	90%	N	N	N	2.7	VD		-	38	0	38.00	N	N	N	N
46	8/18/2017		2	1	69%	N	Y	PROM	2.9	VD		-	36	0	36.00	N	N	N	N

PI > 95
 < 95



RH NEG

EPILEPSY

|RH NEG

|RH NEG

44	22	5/2/2016	12	11/19/2016	2	-	-	1	-	-	no	no	no	164	58	22	12	54	11/12/2016	3	1	1.41	no	2.5	ND	-	-
45	21	5/7/2016	13	11/8/2016	2	1	1	-	-	-	no	no	no	160	54	21	13	67	11/8/2016	2	1	0.62	yes	3.3		lscs	-
46	19	5/7/2016	12	11/16/2016	1	-	-	-	-	-	no	no	no	162	54	20	12	67	11/16/2016	3	1	2.48	no	3.3		lscs	-
47	22	5/7/2016	13	11/11/2016	1	-	-	-	-	-	no	no	no	165	62	21	13	59	11/11/2016	4	1	2.96	no	3.2		lscs	-
48	21	5/16/2016	12	11/19/2016	2	-	-	1	-	-	no	no	no	160	52	21	12	65	11/22/2016	3	1	1.88	no	2.6	ND	-	-
49	20	5/16/2016	13	11/15/2016	1	-	-	-	-	-	no	no	no	156	48	20	13	70	11/19/2016	4	2	1.52	no	2.9	ND	-	-
50	28	5/16/2016	12	11/18/2016	1	-	-	-	-	-	no	no	no	164	60	20	12	64	11/18/2016	3	2	1.44	no	2.6		lscs	-
51	29	5/17/2016	12	11/13/2016	4	2	1	1	-	-	no	no	no	162	54	20	12	61	11/13/2016	4	1	0.91	no	0.88	ND	-	PTD (FSB)
52	27	5/20/2016	12	11/30/2016	2	1	1	-	-	-	no	no	no	166	58	23	12	58	11/30/2016	3	1	1.34	no	2.7	ND	-	-
53	34	5/20/2016	13	11/25/2016	2	1	1	-	-	-	no	no	no	164	55	21	13	73	11/25/2016	3	2	0.67	no	2.6		lscs	-
54	20	5/20/2016	11	11/30/2016	1	-	-	-	-	-	no	no	no	158	52	21	11	43	11/30/2016	3	1	1.8	no	3.1		lscs	-
55	20	5/20/2016	11	11/30/2016	1	-	-	-	-	-	no	no	no	154	56	23	11	43	11/30/2016	3	1	2.1	no	3		lscs	-
56	19	5/23/2016	12	11/27/2016	2	1	1	-	-	-	no	no	no	160	52	20	13	63	11/27/2016	4	1	2.4	no	2.8	ND	-	-
57	24	5/23/2016	12	12/4/2016	2	1	1	-	-	-	no	no	no	164	55	20	12	52	12/4/2016	3	2	1.44	no	2.4	ND	-	-
58	19	5/23/2016	14	11/21/2016	2	-	-	1	-	-	no	no	no	166	54	21	12	63	11/29/2016	3	1	2.19	no	2.3	ND	-	-
59	34	5/23/2016	13	11/24/2016	1	-	-	-	-	-	no	no	no	168	64	23	12	65	12/1/2016	3	1	2.29	no	2.9	ND	-	-
60	29	5/30/2016	12	12/12/2016	2	1	1	-	-	-	no	no	no	162	54	22	12	59	12/12/2016	4	1	1.8	no	3.1		lscs	-
61	22	5/30/2016	12	12/7/2016	2	1	1	-	-	-	no	no	no	160	52	21	12	66	12/7/2016	3	1	1.78	no	1.9		PT lscs (sev oligo)	-
62	21	6/1/2016	13	12/2/2017	2	1	1	-	-	-	no	no	no	162	52	22	13	68	12/2/2017	3	1	1.61	yes	1.2		-	PTD (33wk)
63	27	6/6/2016	12	12/14/2016	2	1	1	-	-	-	no	no	no	166	57	22	12	62	12/14/2016	3	1	0.95	no	2.4	ND	-	-
64	22	6/6/2016	12	12/18/2016	2	1	1	-	-	-	no	no	no	168	64	23	12	59	12/18/2016	4	2	1.43	no	2.8	ND	-	-
65	27	6/6/2016	13	12/8/2016	1	-	-	-	-	-	no	no	no	165	62	21	13	62	12/8/2016	3	1	1.45	no	2.6		lscs	-
66	21	6/13/2016	13	12/14/2016	2	-	-	1	-	-	no	no	no	164	55	21	13	64	12/14/2016	3	2	1.66	no	3		lscs	-
67	24	6/13/2016	12	12/26/2016	1	-	-	-	-	-	no	no	no	166	65	25	12	51	12/26/2016	3	1	2.64	no	3.3	ND	-	-
68	20	6/13/2016	12	12/23/2016	2	-	-	1	-	-	no	no	no	156	58	21	12	66	12/23/2016	3	1	1.05	no	2.7		lscs	-
69	23	6/14/2016	13	12/19/2016	3	1	1	1	-	-	no	no	no	162	55	22	13	72	12/19/2016	3	1	1.06	no	2.8		lscs	-
70	23	6/17/2016	13	12/20/2016	1	-	-	-	-	-	no	no	no	155	52	21	13	78	12/20/2016	3	2	1.88	no	2.4	ND	-	-
71	26	6/17/2016	13	12/10/2016	1	-	-	-	-	-	no	no	no	160	55	22	13	79	12/20/2016	4	1	0.98	no	2.7	ND	-	-
72	31	6/27/2016	12	1/6/2017	2	-	-	1	-	-	no	no	no	164	54	21	12	58	1/6/2017	3	1	2.95	no	2.7		lscs	-
73	22	6/28/2016	13	1/1/2017	1	-	-	-	-	-	no	no	no	160	52	21	13	73	1/1/2017	3	1	1.22	no	2.5		-	-
74	24	7/4/2016	14	12/28/2017	3	1	1	1	-	-	no	no	no	162	58	22	12	60	1/10/2017	3	1	1.88	no	2.4	ND	-	-
75	24	8/1/2016	12	2/13/2017	1	-	-	-	-	-	no	no	no	156	60	23	12	56	2/13/2017	3	1	2.07	no	3	ND	-	-
76	20	8/1/2016	13	2/4/2017	1	-	-	-	-	-	no	no	no	154	56	23	13	76	2/6/2017	3	1	2.98	no	2.4		lscs	-
77	23	8/1/2016	13	1/7/2017	1	-	-	-	-	-	no	no	no	164	55	21	13	62	1/7/2017	2	1	1.62	no	2.8	ND	-	-
78	20	8/1/2016	13	2/2/2017	1	-	-	-	-	-				160	52	22	13	62	2/2/2017	3	0	2.17	no	2.6		lscs	-
79	35	8/5/2016	11	2/13/2017	2	1	1	-	-	-				160	55	22	12	55	2/19/2017	2	1	1.36	no	2.8	ND	-	-
80	22	8/8/2016	12	2/19/2017	1	-	-	-	-	-				158	52	20	12	62	2/19/2017	2	1	1.32	no	3	ND	-	-
81	19	8/8/2016	13	2/6/2017	1	-	-	-	-	-				158	52	21	13	74	2/6/2017	2	1	1.16	no	1.4		-	PTD (FSB-IUD)
82	28	8/8/2016	12	2/13/2017	1	-	-	-	-	-				156	58	21	12	62	2/17/2017	2	1	2.1	no	3.2		lscs	-
83	22	8/22/2016	13	2/25/2017	2	-	-	1	-	-				160	52	21	13	53	3/3/2017	2	1	1.73	no	0.1		-	PTD (symmetrical FGR with encephalocoele)
84	23	8/22/2016	19	1/16/2017	1	-	-	-	-	-				162	55	22	13	78	2/24/2017	2	1	1.78	2.4kg	ND		-	-
85	21	8/26/2016	13	3/2/2017	1	-	-	-	-	-				166	60	23	13	52	3/10/2017	2	1	3	no	2.5	ND	-	-
86	21	8/29/2016	13	2/28/2017	1	-	-	-	-	-				152	58	25	13	75	2/28/2017	2	1	1.97	yes	2.4		lscs	-
87	22	9/2/2016	12	3/14/2017	2	1	1	-	-	-				158	61	24	12	54	3/14/2017	2	1	1.55	no	2.7	ND	-	-
88	21	9/2/2016	8	4/9/2017	1	-	-	-	-	-				162	57	21	11	49	3/18/2017	2	1	0.27	no	2.5	ND	-	-
89	24	9/12/2016	14	3/9/2017	2	1	1	-	-	-				156	54	22	11	49	3/28/2017	2	1	1.4	no	3.01		lscs	-
90	27	9/12/2016	13	3/16/2017	1	-	-	-	-	-				160	54	23	12	61	3/22/2017	2	1	2.1	no	2.6	ND	-	-
91	30	9/17/2016	12	4/1/2017	2	1	1	-	-	-				160	55	22	12	53	4/1/2017	2	1	1.2	no	2.8	ND	-	-
92	25	9/19/2016	11	4/10/2017	1	-	-	-	-	-				147	50	23	11	44	4/4/2017	3	1	0.55	no	2.9		lscs	-
93	24	9/19/2016	11	4/4/2017	1	-	-	-	-	-				160	50	20	11	44	4/4/2017	2	1	1.7	no	2.6		lscs	-
94	28	9/23/2016	11	4/10/2017	4	2	2	1	-	-				164	65	24	11	54	4/10/2017	2	1	1.65	no	2.7	ND	-	-
95	26	9/23/2016	12	4/2/2017	2	1	1	-	-	-				156	25	22	11	49	4/8/2017	3	1	0.22	no	2.6		lscs	-
96	25	9/26/2016	12	4/9/2017	3	1	1	1	-	-				167	60	23	12	61	4/7/2017	2	1	1.89	no	2.8	ND	-	-

97	24	9/26/2016	13	3/31/2017	2	1	1	-	-	-				154	56	23	13	78	3/31/2017	2	1	2.1	no	3.6			lscs	-
98	32	10/8/2016	11	4/23/2017	3	2	1	1	-	-				165	55	21	11	53	4/23/2017	3	1	1.7	no	2.8	ND		-	-
99	29	10/27/2016	13	5/4/2017	2	1	1	-	-	-				160	52	20	13	61	5/4/2017	3	1	1.32	no	2.9			lscs	-
100	28	11/12/2016	12	5/21/2017	1	-	-	-	-	-				158	56	22	12	66	5/21/2017	2	1	1.6	no	3	ND		-	-
101	28	11/17/2016	12	5/29/2017	4	2	1	1	1	-				165	62	23	12	57	5/29/2017	2	1	1.5	no	2.8			lscs	-
102	21	11/17/2016	12	5/30/2017	2	1	1	-	-	-				164	58	22	12	63	5/30/2017	2	1	2.2	no	2.4	ND		-	-
103	26	11/17/2016	13	5/25/2017	2	1	1	-	-	-				166	62	23	13	76	5/25/2017	3	1	1.4	no	3.1	ND		-	-
104	24	11/23/2016	13	5/26/2017	5	3	1	1	-	2				168	62	21	13	77	5/26/2017	3	1	2.4	no	3	ND		-	-
105	23	12/1/2016	12	6/12/2017	2	1	-	-	-	1				158	62	24	12	57	6/12/2017	2	1	1.56	no	2.9			lscs	-
106	27	12/15/2016	12	6/8/2017	2	1	1	-	-	-				158	52	20	12	63	6/12/2017	1	1	1.9	no	3			lscs	-
107	22	12/15/2016	12	6/4/2017	2	1	1	-	-	-				160	50	20	12	59	6/12/2017	3	1	1.87	no	2.8	ND		-	-
108	26	1/6/2017	11	7/14/2017	1	-	-	-	-	-				158	56	22	11	55	7/27/2017	2	1	1.66	no	3			lscs	-
109	28	1/6/2017	13	7/13/2017	1	-	-	-	-	-				148	55	25	13	76	7/13/2017	2	1	1.6	no	2.2			lscs	-
110	21	1/6/2017	13	7/11/2017	1	-	-	-	-	-				150	55	25	13	77	7/11/2017	1	1	3	yes	2.1			lscs	-
111	27	1/7/2017	13	7/15/2017	2	-	-	-	1	-				147	50	23	13	76	7/15/2017	1	1	2.95	yes	3.1	ND		-	-
112	24	1/9/2017	11	7/30/2017	2	1	1	-	-	-				152	55	23	11	45	7/30/2017	2	1	2.6	no	3.1	ND		-	-
113	21	1/19/2017	11	8/5/2017	2	1	1	-	-	-				156	52	21	11	44	8/5/2017	2	1	0.21	no	1.9			PT lscs (PPROM)	-
114	24	1/20/2017	12	8/3/2017	3	2	1	-	-	-				154	56	23	12	62	8/3/2017	1	1	1.01	no	2.9	ND		-	-
115	20	1/20/2017	12	8/3/2017	2	1	1	-	-	-				148	54	25	12	62	8/3/2017	2	1	2.86	no	3.4	ND		-	-
116	32	1/23/2017	11	8/2/2017	3	2	2	-	-	-				160	55	22	11	46	8/2/2017	2	1	1.4	no	2.7	ND		-	-
117	36	1/23/2017	12	8/10/2017	2	1	1	-	-	-				160	52	20	12	44	8/10/2017	2	1	2.8	no	2.7	ND		-	-
118	25	2/2/2017	11	8/18/2017	2	1	1	-	-	-				162	57	21	11	46	8/18/2017	2	1	1.8	no	2.9	ND		-	-

POG (Weeks)	FGR
37weeks	-
38 weeks	-
37 weeks	-
39weeks	yes
38weeks 2days	yes
40 weeks 3 days	-
37 weeks	-
38 weeks 4 days	-
39 weeks 5 days	-
38weeks 5 days	-
37 weeks	-
37 weeks 4days	-
38 weeks	yes
39 weeks	-
38 weeks 1 day	-
38 weeks 5 days	-
38 weeks 2 days	-
39 weeks	-
38 weeks 6 days	-
-	-
38 weeks 4 days	-
39 weeks	-
39 weeks	-
38 weeks 1 day	yes
36 weeks 2 days	-
37weeks 5days	-
36 weeks 2 days	-
40 weeks 2 days	-
21 week 2 days	-
37 weeks 4days	-
38 weeks 4 days	-
37 weeks	-
38 weeks	-
38 weeks 4 days	-
39 weeks	yes
38 weeks	-
40 weeks 2 days	-
38 weeks	-
38 weeks	-
39 weeks	-
40 weeks	-
39 weeks	-
37 weeks	yes

39 weeks 2 days	-
40 weeks 3 days	-
40 weeks 4 days	-
38 weeks 2 days	-
40 weeks 4 days	-
38 weeks 4 days	-
37 weeks	-
25 weeks 4 days	-
38 weeks 6 days	-
39 weeks	-
39 weeks 2 days	-
39 weeks	-
37 weeks	-
39 weeks 3days	yes
38 weeks 1 day	-
40 weeks	-
37 weeks 2 days	-
32 weeks	-
33 weeks	-
39 weeks	yes
40 weeks 5 days	-
38 weeks 4 days	-
40 weeks 3 days	-
41 weeks	-
39 weeks 5 days	-
37 weeks 4 days	-
39 weeks 5 days	-
39 weeks 2 days	-
37 weeks 4days	-
38 weeks	-
39 weeks 5 days	yes
37 weeks 4 days	-
38 weeks	yes
39 weeks	-
38 weeks 1 day	-
39 weeks 5 days	-
40 weeks 2 days	-
22	-
38 weeks 5 days	-
23	-
37 weeks	-
37 weeks 5 day	-
39 weeks 6 days	yes
38 weeks	-
37 weeks 2 days	-
38 weeks 2 days	-
38 weeks 6 days	-
38 weeks	-
39 weeks	-
37 weeks 2 days	-
38 weeks 5 days	-
40 weeks	-
37 weeks 4 days	-

38 weeks 2 days	-
39 weeks	-
38 weeks 2 days	-
37 weeks 4 days	-
37 weeks	-
40 weeks 4 days	yes
40 weeks	-
38 weeks	-
37 weeks 2 days	-
37 weeks 6 days	-
38 weeks	-
39 weeks 2 days	-
39 weeks 3 days	yes
37 weeks 2 days	yes
38 weeks	-
40 weeks 6 days	-
32 weeks 4 days	-
38 weeks	-
38 weeks	-
37 weeks 5 days	-
38 weeks	-
36 weeks	-