

## PREDICTION OF HYPERTENSIVE DISORDERS IN EARLY TRIMESTER OF PREGNANCY

<sup>1</sup>Dr. Shashi Jyothsna Parlapally, <sup>2</sup>Dr. Vanitha CH, <sup>3</sup>Dr. Pilli Rajitha

<sup>1,2,3</sup>Assistant Professor, Department of OBG, Kakatiya Medical College, Warangal, Telangana, India

**Corresponding Author:**

Dr. Vanitha CH

### Abstract

**Background and objectives:** Predicting preeclampsia (PE) at 11-14 weeks of gestation is a new concept. Studies integrating multiple factors at 11-14 weeks of pregnancy have been conducted, but an algorithm with a good predictive value has yet to be created. This study aimed to design a methodology combining MAP, Uterine artery Doppler, and PAPPa at 11-14 weeks of pregnancy to predict PE in India. Basically objective is to determine whether higher Mean Arterial Pressure (MAP), increased Uterine Artery Pulsatility Index (UAPI), and low Pregnancy Associated Plasma Protein A (PAPP - A) between weeks 11-14 of pregnancy are linked to the growth of hypertensive diseases in pregnancy.

**Method:** This is a prospective cohort study. Data were obtained from 200 registered patients attending antenatal OPD in hospitals between 11 and 14 weeks of gestation. MAP, blood pressure, uterine artery Doppler, and serum sample for PAPPa were measured. IBM SPSS Version 22 for Windows was used to analyse the data.

**Result:** There were a total of 200 women enrolled in the study, and 24 of those women (37.1%) suffered difficulties. At 11-14 weeks of pregnancy, the uterine artery doppler pulsatility index (PI) was found to be an effective screening tool (sensitivity 29%, specificity 90%) for the prediction of pregnancy.

**Conclusion:** This study revealed that the uterine artery Doppler Pulsatility index is an effective screening approach for women at high risk of developing preeclampsia and related complications during the 11th to 14th week of pregnancy.

**Keywords:** Pregnancy, Preeclampsia, Gestation, MAP (Mean Arterial Pressure), Uterine Artery Doppler.

### Introduction

One of the most prevalent medical complications that can arise during pregnancy is high blood pressure, which is also one of the major causes of maternal and perinatal mortality<sup>[1-2]</sup>. The prevalence of hypertensive diseases can range anywhere from 5 to 10 percent during pregnancy; however, this number is on the rise since women are delaying their first pregnancy until they are older and are gaining more weight before becoming pregnant. In contrast side, the frequency of eclampsia is decreasing in industrialised and prosperous societies due to improvements in antenatal care and the management of pre-eclamptic states.

This is a direct result of these improvements<sup>[3-4]</sup>. The process of human placentation is dependent on the invasion of trophoblast cells into the maternal decidua, myometrium, and their blood arteries. Cytotrophoblastic cells will invade the maternal spiral artery and partially replace the endothelium of this vessel. This will result in the gradual dilation of these blood vessels. This process starts as early as the tenth day after conception and continues all the way through the nine months of pregnancy. The development of preeclampsia and intrauterine growth restriction (IUGR)<sup>[5]</sup>, both of which are major causes of perinatal morbidity and mortality around the world, are thought to be caused by a major etiological factor that is defective placentation. However, the exact nature of this factor is still up for debate<sup>[6]</sup>. Artery of the uterus According to measurements taken using a Doppler, the impedance to the flow in the uterine artery reduces as the gestational age progresses in a pregnancy that is developing normally. However, this obstruction to flow is exacerbated when preeclampsia and IUGR have already developed<sup>[7-8]</sup>. However, there has been growing evidence that examining the circulation of the uterus during the first trimester might help predict preeclampsia and intrauterine growth restriction (IUGR). As a natural byproduct of the placentation process, placental materials are expelled<sup>[29]</sup>. The levels of these products are reflective of the pathophysiology of abnormal placentation, and as a consequence, they are playing an increasingly important role in early gestation screening tests for later complications of pregnancy<sup>[4]</sup>. These include pregnancy associated plasma protein A (PAPPA), placental growth factor (PIGF), soluble FMSlike tyrosine kinase 1 (sFlt-1), soluble endoglin (s Eng), placental protein 13 (PP13), activating an inhibin A disintegrin and metalloprotease 12, and placental protein 13 (PP13) (ADAM12)<sup>[17]</sup>.

Insulin-like growth factor binding protein 4 is a substrate for the protease known as PAPPA (ILGFBP 4). There is a correlation between a low level of PAPPA and higher levels of ILGFBP 4 and lower levels of free insulin-like growth factor (ILGF). It is well known that insulin-like growth factor can affect foetal growth by modulating the intake of glucose and amino acids, in addition to playing an autocrine and paracrine function in the process of trophoblast invasion. It has been demonstrated that the level of maternal serum PAPPA is relatively low in the first trimester of preeclamptic and/or IUGR-affected pregnancies. As a result, the title of this research paper is "Early trimester prediction of hypertensive diseases in pregnancy utilising Mean arterial pressure (MAP), uterine artery pulsatility index (UAPI), and pregnancy related plasma protein A (PAPPA)." aims to determine the likelihood of hypertension problems occurring during pregnancy between the 11th and 14th weeks of gestation<sup>[9-17]</sup>.

## Materials and Methods

This prospective study was conducted at c km hospital over the course of two years, beginning in June 2020 and ending in may 2022, during which time it enlisted a total of 200 women with singleton pregnancies between 11-14 weeks of gestation. This number includes 200 antenatal women who visited OPD and satisfied the inclusion and exclusion criteria.

## Inclusion criteria

1. Pregnancy with a single baby
2. Gestational age between 11 and 14 weeks of pregnancy

## Exclusion criteria

1. Multiple pregnancies
2. Individuals who have a history of preeclampsia, diabetes mellitus, chronic hypertension, renal illness, autoimmune disease, vasospastic or immunological problems in their medical history.

## Procedure

The most accurate dates from the woman's menstrual history and an early ultrasound will be used to determine the gestational age of the baby. Every woman was asked extensive questions about her age, parity, previous obstetric history, medical history, and family history. Additionally, her height, weight, and blood pressure were all assessed.

## Mean arterial pressure

Two digital sphygmomanometers (model HEM-7121, Omron healthcare Co., Ltd., Japan) with standard (22 to 32cm) adult cuffs were used to measure blood pressure in both arms concurrently in a sitting position with the arms supported at heart level. Following 5 minutes of rest, blood pressure was measured and a sequence of recordings were made at one-minute periods until the difference between two successive readings was within 10 mmHg in systolic BP and 6mmHg in diastolic BP in both arms <sup>[17]</sup>.

## Uterine artery Doppler

Uterine artery Doppler was done according to the ISUOG practice guidelines (2013) for use of Doppler Ultrasonography in obstetrics. The crown rump length and biparietal diameter were taken transvaginally, and the placenta was localised. A uterine midsagittal slice was taken, and the cervical canal was detected. The probe was then advanced laterally until the paracervical vascular plexuses were visible, colour Doppler was activated, and the uterine artery was detected as it ascended the uterine body while turning cranially. At this stage, before the uterine artery branched into the arcuate arteries, measurements were obtained, and the operation was repeated on the opposite side. The pulsatility index (PI) was measured bilaterally, and the average PI of the uterine arteries was computed. 11-week cutoff for uterine pulsatility index was >1.6, 12-week cutoff was >1.5, and 13-week cutoff was >1.4 <sup>[24-28]</sup>.

## Maternal serum samples

Samples of maternal serum were obtained via venepuncture. The specimens were centrifuged, and the serum was placed in a deep freezer (-200C) Cut off for PAPP A was taken as at, 11week <0.8 m IU/ml, 12week <1.03m IU/ml, 13week<1.47m IU/ml.

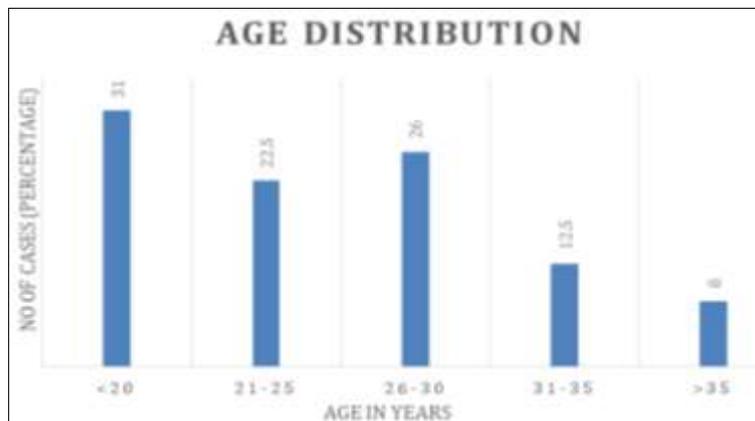
These women were followed up at an ANC clinic and assessed every four weeks until they were 28 weeks pregnant, then every two weeks until they were 34 weeks pregnant, and then weekly until delivery and for up to 12 weeks following delivery. Cases in whom the screening test returns a positive result are carefully watched, and, if necessary, early

intervention is provided in order to reduce the risk of problems <sup>[11]</sup>.

## Results and observation

**Table 1:** Age distribution of the patients

Sr. No	Age years	Percentage	Frequency
1	<20	31	62
2	21-25	22.5	45
3	26-30	26	52
4	31-35	12.5	25
5	>35	8	16
Total		100	200



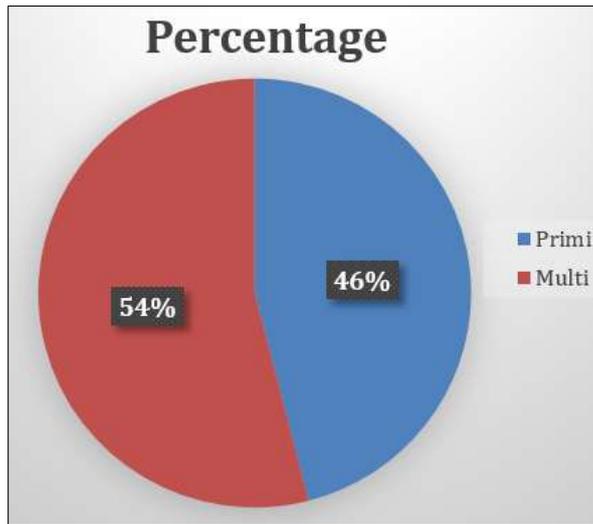
**Graph 1:** Graphical presentation of age distribution

31% Patients from age group <20, 22.5% patients are in the age group 21-15 years only, 8% are in the age group of >31 years.

## 2. Parity distribution

**Table 2:** Parity distribution

Sr. No	Gravida	Frequency	Percentage
1	Primi	46	92
2	Multi	54	108
Total		200	100

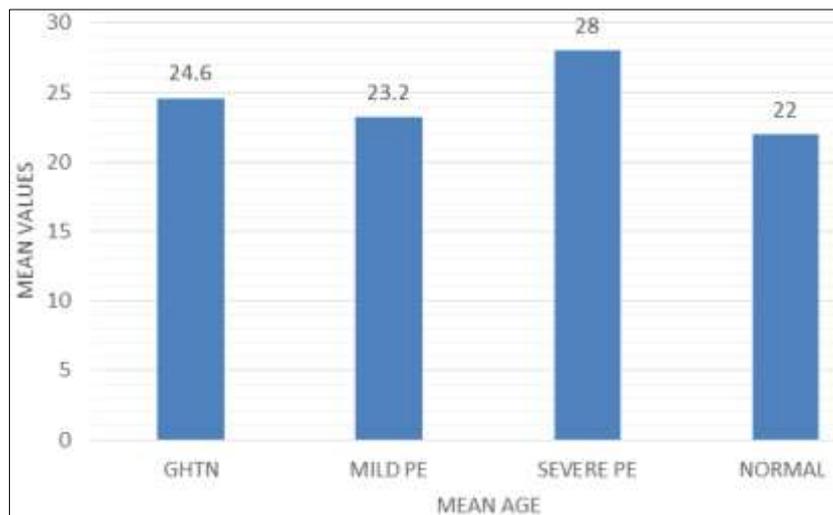


**Graph 2:** Pie chart of parity distribution

**Table 3:** Mean age distribution of the subjects based on the outcome

Sr. No	Outcome	No of patients	Mean age	STD deviation
1	GHTN	8	24.6	3
2	Mild PE	12	23.2	2.5
3	Severe PE	8	28	3.15
4	Normal	172	22	3.45

Anova  $p < 0.345$ , NS

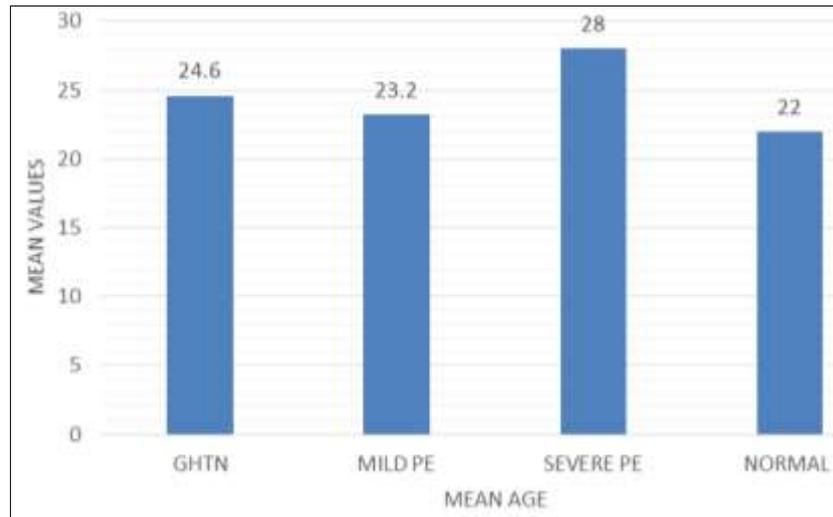


**Graph 3:** Mean age distribution of the subjects based on the outcome

Mean age of the women WHO Not developed PE is 22 years. Mean age of the women developed GHTN, MILD PE, SEVERE PE is 24.67 years, 23.21 years, 28 years respectively

**Table 4:** Blood pressure frequency in study

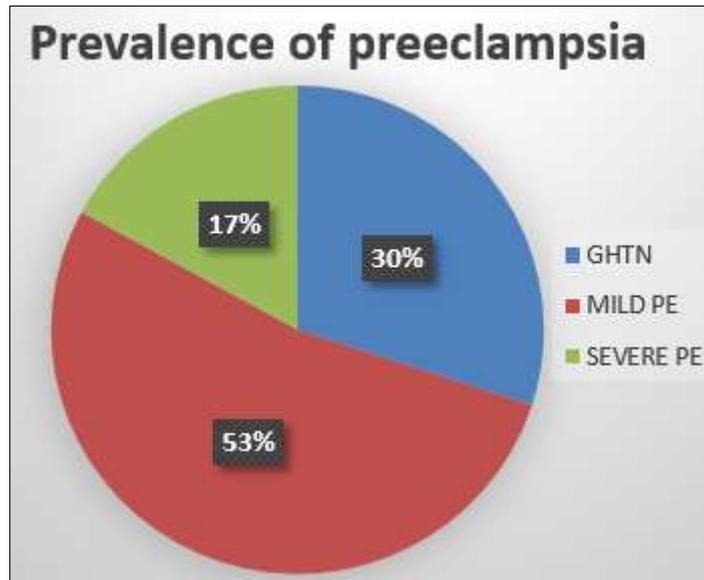
Blood pressure		Frequency	Percentage
SBP	<140	174	87
	>140	26	13
DBP	<90	174	87
	>90	26	13

**Fig 4:** Blood pressure measurement in study

Out of 200 women, 13% of women had raised SBP and DBP

**Table 5: Prevalence of preeclampsia**

Sr. No	Condition	No of subjects
1	GHTN	8
2	Mild PE	12
3	Severe PE	4
Total		

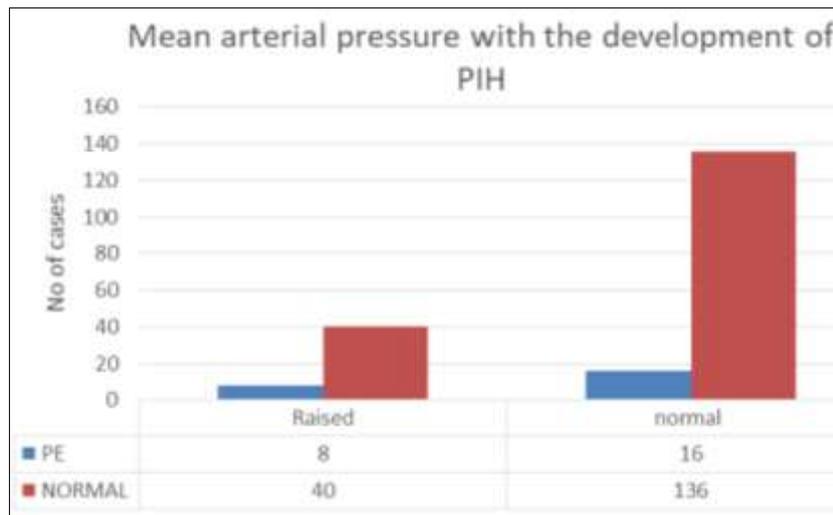


**Graph 5:** Prevalence of preeclampsia

Prevalence of preeclampsia - 30% GHTN, 53% mild PE, 17% severe PE

**Table 6:** Mean arterial pressure with the development of PIH

Sr. No	MAP		Total
	Raised	Normal	
PE	8	16	24
Normal	40	136	176
Total	48	152	200



**Graph 6:** Mean arterial pressure with the development of PIH

## Discussion

In our two-year observational research of 200 women, mean arterial pressure (MAP), uterine artery pulsatility index (UAPI), and pregnancy associated plasma protein A (PAPPA) at 11-14 weeks of gestation were analysed. These patients were monitored until delivery, and details of their pregnancy and delivery were recorded. 8 percent of the 200 women studied developed preeclampsia. The prevalence of hypertensive disorders during pregnancy in India was 7.9%, with preeclampsia occurring in 5.6% of the studied population. 26% of 200 women with elevated MAP had PIH, which is comparable to the 3% of women with elevated MAP at 11-14 weeks of gestation documented by Poon LC *et al.* Kuc *et al.* observed in a nested case-control research conducted in the Netherlands that first trimester MAP is one of the most significant predictors of preeclampsia. In the present study, however, the predictive power of MAP is statistically insignificant (p value 0.852) when compared to non-PIH patients; therefore, this will not aid in the prediction of PIH, similar to the study by Shinjini Narang *et al.* with comparable results (p 0.719). Although a low PAPPV alone is not a good signal of preeclampsia, research have shown that combining first trimester PAPPV with Uterine artery Doppler velocimetry significantly improves detection [10-12]. PAPPV alone at 11-14 weeks could not predict PIH in our study (p value 0.445), but when paired with MAP (p value 0.000) and UAPI (p value 0.03), sensitivity increased to 67% and 75%, respectively. The accuracy of uterine artery Doppler analysis in the first trimester for predicting IUGR and preeclampsia was evaluated in a recent meta-analysis by Velauthar *et al.* 72 Evaluation of eighteen trials involving 55,974 women, of which fifteen enrolled women with low-risk pregnancies. The aberrant flow velocity waveforms were defined by a uterine artery RI or PI greater than the 90th percentile and the presence of notching (unilateral/bilateral). With a sensitivity of 26.4%, an aberrant uterine artery pulsatility index in the first trimester was predictive of preeclampsia. In the present study, the uterine artery pulsatility index at 11-14 weeks of pregnancy was revealed to be the most accurate predictor of preeclampsia due to its high sensitivity (29%) and specificity (90%). Therefore, the uterine artery pulsatility index alone is a good screening test for the prediction of preeclampsia in the first trimester, particularly in a developing country like India where resources are limited. 87.3% of births were vaginal (15.5% preterm, 82.5% term), whereas 11.5% were caesarean sections.

## Conclusion

In this study, preeclampsia was not linked to MAP. Low PAPPV isn't a good predictor of preeclampsia; uterine artery Doppler velocimetry improves identification. PAPPV wasn't predictive of preeclampsia in this study. In the current study, uterine artery PI at 11-14 weeks of pregnancy was determined to be the best indicator for screening women at risk of developing preeclampsia. It had sensitivity (28%) and specificity (92%) for identifying the high risk group at the above specified gestational age cutoff.

**Conflict of Interest:** None

**Funding Support:** Nil

**References**

1. Poon LC, Kametas NA, Maiz N, Akolekar R, Nicolaides KH. First-trimester prediction of hypertensive disorders in pregnancy. *Hypertension*. 2009;53(5):812-818.
2. Shand AW, Whitton K, Pasfield A, Nassar N, McShane M, Han X, *et al.* Evaluation of anti-Mullerian hormone in the first trimester as a predictor for hypertensive disorders of pregnancy and other adverse pregnancy outcomes. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2014;54(3):244-249.
3. Papageorghiou AT, Campbell S. First trimester screening for preeclampsia. *Current Opinion in Obstetrics and Gynecology*. 2006;18(6):594-600.
4. Uzan J, Carbonnel M, Piconne O, Asmar R, Ayoubi JM. Pre-eclampsia: pathophysiology, diagnosis, and management. *Vascular health and risk management*. 2011;7:467.
5. Scazzocchio E, Figueras F. Contemporary prediction of preeclampsia. *Current Opinion in Obstetrics and Gynecology*. 2011;23(2):65-71.
6. Fisher SJ, McMaster M, Roberts JM. The placenta in normal pregnancy and preeclampsia. In *Chesley's hypertensive disorders in pregnancy*. Academic Press, 2015, 81-112.
7. Park FJ, Leung CH, Poon LC, Williams PF, Rothwell SJ, Hyett JA. Clinical evaluation of a first trimester algorithm predicting the risk of hypertensive disease of pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2013;53(6):532-539.
8. Ohkuchi A, Hirashima C, Takahashi K, Suzuki H, Matsubara S. Prediction and prevention of hypertensive disorders of pregnancy. *Hypertension Research*. 2017;40(1):5-14.
9. Angeli F, Angeli E, Reboldi G, Verdecchia P. Hypertensive disorders during pregnancy: clinical applicability of risk prediction models. *Journal of hypertension*. 2011;29(12):2320-2323.
10. Steel SA, Pearce JM, McParland P, Chamberlain GVP. Early Doppler ultrasound screening in prediction of hypertensive disorders of pregnancy. *The Lancet*. 1990;335(8705):1548-1551.
11. Kuc S, Wortelboer EJ, van Rijn BB, Franx A, Visser GH, Schielen PC. Evaluation of 7 serum biomarkers and uterine artery Doppler ultrasound for first-trimester prediction of preeclampsia: a systematic review. *Obstetrical & gynecological survey*. 2011;66(4):225-239.
12. Gómez O, Figueras F, Fernández S, Bennasar M, Martínez JM, Puerto B, *et al.* Reference ranges for uterine artery mean pulsatility index at 11–41 weeks of gestation. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2008;32(2):128-132.
13. Vainio M, Kujansuu E, Koivisto AM, Maenpaa J. Bilateral notching of uterine arteries at 12-14 weeks of gestation for prediction of hypertensive disorders of pregnancy. *Acta obstetrica et gynecologica Scandinavica*. 2005;84(11):1062-1062.
14. Poon, L. C. Y., Kametas, N. A., Chelemen, T., Leal, A., & Nicolaides, K. H. (2010). Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. *Journal of human hypertension*, 24(2), 104-110.
15. Angeli E, Verdecchia P, Narducci P, Angeli F. Additive value of standard ECG for the risk prediction of hypertensive disorders during pregnancy. *Hypertension Research*. 2011;34(6):707-713.
16. Hanchard TJ, de Vries BS, Quinton AE, Sinosich M, Hyett JA. Ultrasound features prior

- to 11 weeks' gestation and first-trimester maternal factors in prediction of hypertensive disorders of pregnancy. *Ultrasound in Obstetrics & Gynecology*. 2020;55(5):629-636.
16. Chen Y, Wang X, Hu W, Chen Y, Ning W, Lu S, *et al*. A risk model that combines MAP, PlGF, and PAPP-A in the first trimester of pregnancy to predict hypertensive disorders of pregnancy. *Journal of Human Hypertension*. 2022;36(2):184-191.
  17. Sibai BM. Hypertensive disorders of pregnancy: the United States perspective. *Current Opinion in Obstetrics and Gynecology*. 2008;20(2):102-106.
  18. Sibai BM. First-trimester screening with combined maternal clinical factors, biophysical and biomarkers to predict preterm pre-eclampsia and hypertensive disorders: are they ready for clinical use. *BJOG*. 2015;122(3):282-283.
  19. Skråstad RB, Hov GG, Blaas HGK, Romundstad PR, Salvesen KÅ. A prospective study of screening for hypertensive disorders of pregnancy at 11-13 weeks in a Scandinavian population. *Acta obstetrica et gynecologica Scandinavica*. 2014;93(12):1238-1247.
  20. Folk DM. Hypertensive disorders of pregnancy: overview and current recommendations. *Journal of midwifery & women's health*. 2018;63(3):289-300.
  21. Akolekar R, Minekawa R, Veduta A, Romero XC, Nicolaides KH. Maternal plasma inhibin A at 11–13 weeks of gestation in hypertensive disorders of pregnancy. *Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis*. 2009;29(8):753-760.
  22. Spencer K, Cowans NJ, Chefetz I, Tal J, Meiri H. First-trimester maternal serum PP-13, PAPP-A and second-trimester uterine artery Doppler pulsatility index as markers of pre-eclampsia. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2007;29(2):128-134.
  23. Velauthar L, Plana MN, Kalidindi M, Zamora J, Thilaganathan B, Illanes SE, *et al*. First-trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55 974 women. *Ultrasound in Obstetrics & Gynecology*. 2014;43(5):500-507.
  24. Pilalis A, Souka AP, Antsaklis P, Basayiannis K, Benardis P, Haidopoulos D, *et al*. Screening for pre-eclampsia and small for gestational age fetuses at the 11–14 weeks scan by uterine artery Dopplers. *Acta obstetrica et gynecologica Scandinavica*. 2007;86(5):530-534.
  25. Khalil AA, Cooper DJ, Harrington KF. Pulse wave analysis: a preliminary study of a novel technique for the prediction of pre-eclampsia. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2009;116(2):268-277.
  26. Spencer K, Cowans NJ, Chefetz I, Tal J, Kuhnreich I, Meiri H. Second-trimester uterine artery Doppler pulsatility index and maternal serum PP13 as markers of pre-eclampsia. *Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis*. 2007;27(3):258-263.
  27. Afrakhteh M, Moeini A, Taheri MS, Haghhighatkah HR, Fakhri M, Masoom N. Uterine Doppler velocimetry of the uterine arteries in the second and third trimesters for the prediction of gestational outcome. *Revista Brasileira de Ginecologia e Obstetrícia*. 2014;36:35-39.
  28. Arthuis CJ, Novell A, Escoffre JM, Patat F, Bouakaz A, Perrotin F. New insights into uteroplacental perfusion: quantitative analysis using Doppler and contrast-enhanced ultrasound imaging. *Placenta*. 2013;34(5):424-431.
  29. Carbillon L. First trimester uterine artery Doppler for the prediction of preeclampsia and foetal growth restriction. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2012;25(7):877-883.