Section: Obstetrics & Gynecology

Research

EARLY TRIMESTER PREDICTION OF HYPERTENSIVE DISORDERS IN PREGNANCY

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Abstract

Background: To investigate the relationship between the emergence of hypertensive disorders in pregnancy and changes in mean arterial pressure (MAP), uterine artery pulsatality index (UAPI), and pregnancy-associated plasma protein A (PAPPA) throughout 11–14 weeks of pregnancy. **Materials and Methods:** The Department of Obstetrics and Gynecology Dr Pinnamaneni Institute of Medical Sciences undertook a prospective cohort study. The 250 patients who visited the antenatal OPD between 11- and 14-weeks' gestation were the source of the data. A serum sample for PAPPA testing, a blood pressure reading, and a uterine artery Doppler were all performed. Preeclampsia was predicted using the uterine artery Pulsatality Index (PI) at 11–14 weeks of pregnancy (sensitivity 29%, specificity 90%, cutoff at 95th percentile to the respective gestational age). Using IBM SPSS Version 22 for Windows, the data was examined. **Result:** Of the 250 women who participated, 55 (22%) experienced complications. At 11–14 weeks of pregnancy, the uterine arterial doppler pulsatality index (PI) was found to be a reliable screening tool (sensitivity: 28%, specificity: 91%) for detecting pregnancy. **Conclusion:** According to the results of this study, uterine artery Doppler Pulsatality Index is an effective screening tool for pregnant women who are at a high risk of developing preeclampsia and its consequences between weeks 11 and 14.

INTRODUCTION

One of the most frequent medical complications during pregnancy is hypertension, which is also one of the main causes of maternal and perinatal mortality. The invading trophoblast ensures that the uterine spiral arteries undergo the vascular remodelling essential to generate the physiological increase in blood supply to the intervillous space required for pregnancy during a normal pregnancy.[1,2] This process starts as early as the tenth day after conception and lasts the entire pregnancy. As a result, these spiral arteries experience a number of modifications that alter them from small diameter, high resistance vessels to low resistance, nonresponsive channels. Preeclampsia and foetal growth limitation may later emerge in some cases as a result of faulty trophoblast invasion and an insufficient maternal vascular response to placentation. The uteroplacental circulation in these pregnancies continues to be in a state of high resistance, which results in generalised endothelial cell damage.[2,3] Vasospasm occurs in the tiny arterioles of the uteroplacental compartment as well as other systemic vascular beds as a result of impaired local synthesis of vasoactive substances such prostaglandins, endothelins, and nitric oxide.

A disproportionate rise following the systemic vasopressor reaction, which impairs renal function and raises total peripheral resistance, hypertension is next brought on. Elevated capillary permeability, platelet thrombosis, and increased vascular tone result from activated or damaged endothelial cells losing their capacity to maintain vascular integrity. Small arteries experience an atherosclerotic-like process as a result of further vascular wall deterioration. The placenta, renal cortex, hepatic lobules, and central nervous system are all affected locally by ischemia and necrosis as a result of all this activity. Due to women delaying their first pregnancies until later in life and gaining more weight before getting pregnant, the frequency of hypertensive disorders in pregnancy ranges from 5 to 10% and is on the rise. On the other hand, due to improved antenatal care and preeclampsia management, the incidence of eclampsia is reducing in the industrialised and wealthy society.[3,4]

The trophoblastic invasion of the maternal decidua, myometrium, and associated blood arteries is

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necessary for human placentation. The endothelium of the maternal spiral artery is invaded and partially replaced by cytotrophoblastic cells, which causes these vessels to progressively enlarge. This procedure starts on the tenth day after conception and lasts the entire pregnancy. Pre-eclampsia and intrauterine growth restriction (IUGR), both of which are major causes of perinatal morbidity and mortality globally, are thought to arise as a result of defective placentation ovarian artery. In a typical pregnancy, Doppler tests reveal that the resistance to the flow in the uterine artery decreases with gestational age. But established preeclampsia and IUGR worsen this flow impedance.[4,5]

However, there have been more and more reports of examining uterine circulation in the first trimester to forecast preeclampsia and IUGR. The placentation process involves the release of placental products. These compounds' levels play a growing role in early gestation screening tests for complications in subsequent pregnancies because they reflect the pathophysiology of faulty placentation. These include placental growth factor (PIGF), metalloprotease 12, soluble FMSlike tyrosine kinase 1 (sFlt-1), soluble endoglin (s Eng), placental protein 13 (PP13), activating A inhibin A disintegrin, and pregnancy-associated plasma protein A (PAPPA) (ADAM12).[5,6]

PAPPA is a protease that breaks down ILGFBP4, or insulin-like growth factor binding protein. Higher ILGFBP 4 and lower free insulin-like growth factor are linked to low PAPPA levels (ILGF). It is well known that insulin like growth factor affects foetal growth by regulating glucose and amino acid intake as well as playing an autocrine and paracrine function in trophoblast invasion.[7,8] Pregnancies complicated by preeclampsia and/or IUGR have been observed to have comparatively low levels of maternal serum PAPPA in the first trimester.The study's title, "Early trimester prediction of hypertensive disorders in pregnancy using Mean arterial pressure(MAP), uterine artery pulsatality index(UAPI), and pregnancy related plasma protein A (PAPPA)," reflects this. is intended to concentrate on the 11–14 week gestational period, hypertension problems in pregnancy, and their prediction.[8,9]

MATERIALS AND METHODS

250 pregnant women who were admitted to the Dr. Pinnamaneni Institute of Medical Sciences for 2 years from June 2020 to July 2022 were the subjects of a hospital-based prospective screening study. The frequency and percentage forms of qualitative data were used. In cases where the P value of the chi square test was invalid due to tiny counts, the association between qualitative variables was evaluated using the Fishers exact test for all 2 x 2 tables and the Chi Square test with continuity correction for 2 x 2 tables. For continuous variables, mean and Sd values were determined. ANOVA was used to assess means. Sensitivity, specificity, PPV, and NPV calculations were made to evaluate the accuracy. Statistics were considered significant at a P value of 0.05 or lower. Data analysis was done using Windows-based IBM SPSS Version 22.

Inclusion Criteria

Women with,

1. Singleton pregnancy
2. Gestational age of 11-14 week of gestation

Exclusion Criteria

Women with,

1. Multiple pregnancy
2. Subjects with past history of preeclampsia, diabetes mellitus, chronic hypertension, renal disease, autoimmune disease, vasospastic or immunological disorders

RESULTS

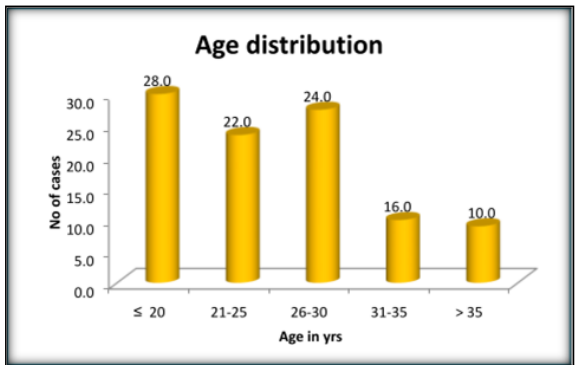

Figure 1: Age distribution in the patients in the study(years)

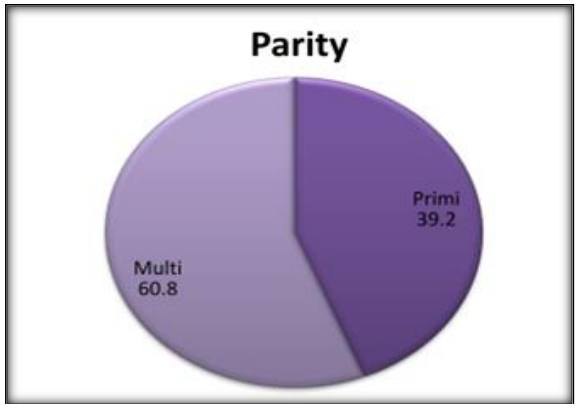

Figure 2: Parity distribution

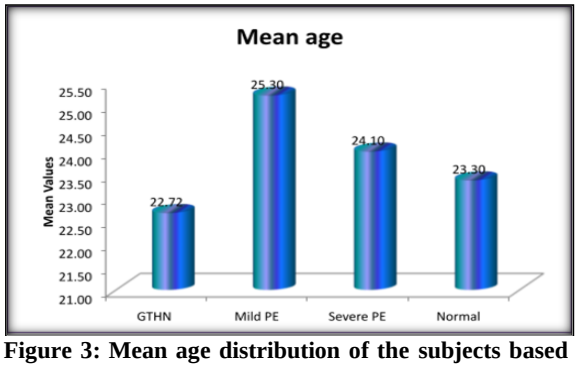

Figure 3: Mean age distribution of the subjects based on the outcome

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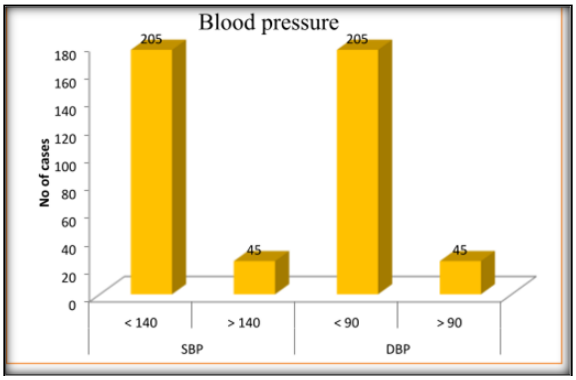

Figure 4: Blood pressure in the study group at the time of diagnosis

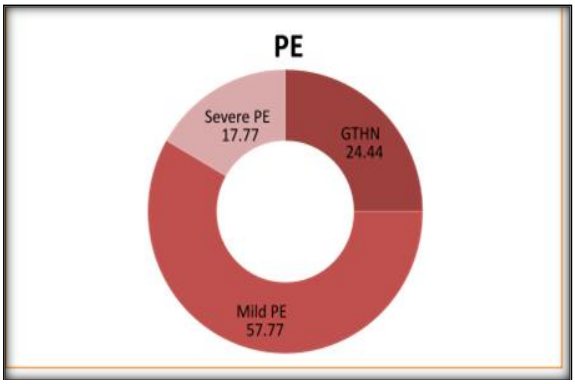

Figure 5: Prevalence of preeclampsia

Table 1: Age distribution of the patients in the study

Age (years)	Frequency	Percentage
<20	70	28
21-25	55	22
26-30	60	24
31-35	40	16
>35	25	10
Total	250	100

22.0% patients are in the age group 21-15 years only, 24 % are in the age group of >31 years.

Table 2: Parity distribution

Gravida	Frequency	Percentage (%)
PRIMI	98	39.2
MULTI	152	60.8
Total	250	100

39.2 % of the patients are primigravida

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

Outcome	No of patients	Mean age	Std. Deviation
GHTN	15	22.72	3.50
MILD PE	38	25.30	2.83
SEVERE PE	11	24.10	3.27
NORMAL	186	23.30	3.79
ANOVA P<0.317,S			

Mean age of the women who didn't developed PE is 23.30 years. Mean age of the women who developed GHTN, MILD PE, SEVERE PE is 22.72 years, 25.30 years, 24.10 years respectively.

Table 4: Blood pressure in study group at the time of diagnosis

Blood pressure		Frequency	Percentage
SBP	<140	205	82
	>140	45	18
DBP	<90	205	82
	>90	45	18

Out of 250 women, 18 % of women had raised SBP and DBP.

Table 5: Prevalence of preeclampsia

Condition	No of subjects	Percentage
GHTN	11	24.44
Mild PE	26	57.77
Severe PE	8	17.77
Total	250	100

Prevalence of preeclampsia – 24.44 % GHTN, 57.77%mild PE, 17.77%severe PE

Table 6: Association of mean arterial pressure with the development of PIH

OUTCOME	MAP		TOTAL
	Raised	Normal	
PE	17	38	55
NORMAL	46	149	195
TOTAL	63	187	250
P <0.952,NS			

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Out of 55 women who developed PIH, 38 women had normal MAP, 17 women had raised MAP. And the p value obtained is <0.952, which is non significant.

Table 7: Association of Pulsatality index with the patients who developed PIH

OUTCOME	UA PI		TOTAL
	Raised	Normal	
PE	8	47	55
NORMAL	55	140	195
TOTAL	63	187	250
P<0.0000, HS			

Out of 55 women who developed PIH, 8 women had raised UAPI, 47 women had normal UAPI. And the p value obtained is <0.000, which is highly significant.

Table 8: Association of the PAPPA with the women who developed PIH

OUTCOME	PAPPA		Total
	Decreased	Normal	
PE	10	45	55
NORMAL	62	133	195
TOTAL	72	178	250
P<0.455, NS			

Out of 55 women who developed PIH, 10 women had decreased PAPPA, 45 women had normal PAPPA. And the p valve is <0.455 which is non significant.

Table 9: Role of mean arterial pressure in predicting PIH

Study variable	Sensitivity	Specificity	PPV	NPV	Accuracy
MAP	11%	85%	23%	76%	69.50%

Mean arterial pressure at 11-14 week of gestation has 85% specificity, 76% NPV. And is 69.50% accurate in predicting PIH at 11-14 weeks.

Table 10: Role of uterine artery pulsatality index in prediction of PIH

Study variable	Sensitivity	Specificity	PPV	NPV	Accuracy
UAPI	28%	91%	28%	92%	83.00%

Uterine artery pulsatality index at 11-14 weeks of gestation has specificity of 91%, NPV of 92%. And is 83.00% accurate in predicting PIH at 11-14 weeks.

Table 11: Role of PAPPA in prediction of PIH

Study variable	Sensitivity	Specificity	PPV	NPV	Accuracy
PAPPA	8%	85%	21.5%	73%	68%

Pregnancy associated plasma protein A at 11-14 weeks of gestation has specificity 85%, NPV is 73%. Accuracy of PAPPA is 68% in predicting the PIH at 11-14 weeks.

Table 12: Comparison of MAP and UAPI in prediction of PIH

UAPI	MAP		Total
	Raised	Normal	
Raised	5	50	55
Normal	47	148	195
Total	52	198	250
P value<0.03, HS			

Study variable	Sensitivity	specificity	PPV	NPV	Accuracy
MAP and UAPI	3%	85%	3%	74%	64.50%

Out of 55 patients, who developed PE 5 patient had both raised MAP and UAPI. When combined MAP and UAPI in prediction of PIH has specificity of 85%, NPV 74%, which is 64.5% accurate, with p valve of <0.03, which is significant.

Table 13: Comparison of MAP and PAPPA in prediction of PIH

PAPPA	MAP		Total
	Raised	Normal	
Decreased	3	52	55
Normal	48	147	195
Total	51	199	250
P value <0.000 HS			

Study variable	Sensitivity	Specificity	PPV	NPV	Accuracy
MAP and PAPPA	3%	78%	4%	72%	58.50%

Out of 55 patients, who developed PE 5 patient had both raised MAP and PAPPA. When MAP and PAPPA were combined in predicting PIH, we got specificity of 78%, NPV of 72%, which are 58.50% accurate in prediction of PIH, with P value of <0.000, which is highly significant.

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Table 14: Comparison of UAPI and PAPPA in predicting PIH

UAPI	PAPPA		Total
	Decreased	Normal	
Raised	4	51	55
Normal	50	145	195
Total	54	196	250
P <0.03, HS			

Study variable	Sensitivity	Specificity	PPV	NPV	Accuracy
UAPI and PAPPA	3%	84%	3%	72%	64%

Out of 55 patients, who developed PE 4 patient had both raised PAPPA and UAPI. When UAPI and PAPPA combined in prediction of PIH, it has specificity if 84%, NPV of 72%, with 64% accuracy, which got the p valve <0.03, which is significant.

Table 15: Distribution of subjects based on mode of delivery

Outcome	Frequency	Percent
Elective LSCS	8	3.2
Emergency LSCS	20	8
FTND	30	12
FTVD	3	1.2
FTVD with vaccum	10	4
FTVD with RMLE, vaccum	5	2
FTVD with assisted breech	2	0.8
FTVD with outlet forceps	15	6
FTVD with RMLE	115	46
PTVD	3	1.2
PTVD with assisted breech	4	1.6
PTVD with RMLE	35	14
Total	250	100

88.5% women had vaginal delivery, 3.2% women had elective LSCS and 8% women had emergency LSCS

Table 16: Analysis of Gestational age at the time of delivery

Gestational age	Outcome		Total
	PE	Normal	
Preterm (<37 weeks)	10	55	65
Term (>37 weeks)	25	160	185
Total	35	215	250
Chi square test p <0.07, NS			

Out of 65 women with PIH, 10 delivered a preterm baby, 55 women delivered at term.

DISCUSSION

In our observational study, 250 women who were receiving antenatal care at OBG outpatient department during a two-year period had their mean arterial pressure (MAP), uterine artery pulsatality index (UAPI), and pregnancy-associated plasma protein A (PAAPA) levels checked. These patients were monitored up until birth, and information on the pregnancy events and delivery method was recorded.[10,11]

250 women were investigated, and preclampsia struck 8% of them. According to a study, preeclampsia affected 5.4% of the studied population in India, and the prevalence of hypertensive disorders during pregnancy was 7.8%. Comparable to Poon LC et al., who reported PIH in 3% of the women with elevated MAP at 11–14 weeks of gestation, 23% of the 250 women had raised MAP and went on to develop PIH.[11,12] First trimester MAP was discovered to be one of the most significant predictors of preeclampsia in a nested case control study conducted in the Netherlands by Kuc et al.[12,13] However, the capacity of MAP to predict PIH in the current study is statistically negligible (p value = 0.952) when compared to non-PIH patients, which is like the study by Shinjini Narang et al. with similar outcomes (p = 0.819).[14,15] Although a low PAPPA by itself is not a reliable diagnostic of preeclampsia, research have shown that combining first trimester PAPPA with uterine artery Doppler velocimetry significantly improves detection. PAPPA at 11–14 weeks does not reliably predict PIH in our study (p value = 0.455), but when paired with MAP and UAPI, sensitivity increased to 78% and 84%, respectively.[16,17]

The effectiveness of uterine artery Doppler analysis in the first trimester in the prediction of IUGR and preeclampsia was recently reviewed by Velauthar et al. A total of 55,974 women were participants in 18 studies, 15 of which included low-risk pregnant women.[18] The aberrant flow velocity waveforms were defined as uterine artery RI or PI >90th percentile and the presence of notching (unilateral/bilateral). With a sensitivity of 26.4%, an aberrant uterine artery pulsatality index in the first trimester was a predictor of preeclampsia. The uterine artery pulsatality index at 11–14 weeks of pregnancy, which exhibited high sensitivity (28%) and specificity (91%) for identifying the high-risk group, was shown to be the best indicator for preeclampsia prediction in the current study.[18,19]

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Therefore, the uterine artery pulsatality index alone is an effective screening test for the early detection of preeclampsia, particularly in a resource-constrained developing country like India. 8.85% of women gave birth vaginally (16.5% preterm, 83.5% term), while 10.5% underwent caesarean sections.[19,20]

CONCLUSION

A complex clinical illness involving several organ systems, perinatal mortality, and morbidity is preeclampsia. Finding the ideal prediction test and preventive measure is still difficult. When compared to mean arterial pressure and PAPPA, the first trimester uterine artery pulsatality index is quite sensitive in predicting PIH and can be utilised as a predictor of preeclampsia. First trimester MAP was discovered to be one of the most significant predictors of PIH in a nested case control study conducted in the Netherlands by Kuc et al. In this investigation, we did not discover a link between MAP and preeclampsia development. Low PAPPA by itself is not a reliable predictor of preeclampsia, however studies have previously shown that combining low PAPPA with uterine artery Doppler velocimetry in the first trimester significantly increases the likelihood of diagnosis. PAPPA was not found to be predictive of preeclampsia in the current investigation.

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