Arterial Resistance in Late First Trimester as a Predictor of Subsequent Pregnancy-Related Hypertension

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المقاومة الشريانية في أواخر الأشهر الثلاثة الأولى من الحمل باعتباره مؤشرا لاحقا على ارتفاع ضغط الدم المرتبط بالحمل

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ABSTRACT: Objectives: This study aimed to examine the association between indicators of arterial resistance occurring late in the first trimester and the subsequent development of pregnancy-related hypertension. Methods: This study took place between May 2014 and August 2015 and included 329 consecutive women with singleton pregnancies attending the antenatal clinics of a medical college in Karnataka, India, during this period. Pulse pressure (PP) and uterine artery Doppler parameters were recorded between 11-14 gestational weeks. Consequently, women were followed-up until after delivery for subsequent hypertension. Results: Hypertension occurred more frequently if PP was high (17.6% versus 14.4% of pregnancies without high PP; P = 0.713), if a diastolic notch (DN) was present (15.1% versus 12.8% of pregnancies with an absent DN; P = 0.612) and if the resistive index (RI) was raised (22.2% versus 14.3% of pregnancies without raised RI; P = 0.366). A raised pulsatility index (PI) was significantly associated with hypertension (P = 0.013). The risk of hypertension was approximately seven-fold higher if two or more arterial resistance indicators were used, except with a present DN plus a raised RI or a present DN plus high PP. All arterial resistance indicators showed negative predictability (>85.6%) and good specificity (≥95.0%), except for the presence of a DN. A population-specific cut-off PI value of 1.72 had high negative predictability (92.8%) and good sensitivity (70.8%) and specificity (65.1%). Conclusion: Raised PI in the late first trimester was a significant predictor of hypertension later in pregnancy. A combination of arterial resistance indicators may enhance prediction of subsequent hypertension.

Keywords: Vascular Resistance; Pulse Pressure; Uterine Artery; Doppler Ultrasonography; Pregnancy-Induced Hypertension; India.

الملخص: الهدف: هدفت هذه الدراسة إلى فحص العلاقة بين عدد من مؤشرات المقاومة الشريانية التي تحدث في وقت متأخر في الأشهر الثلاثة الأولى من الحمل وارتباطها بحدوث ارتفاع ضغط الدم لاحقا. الطريقة: أجريت هذه الدراسة في الفترة ما بين مايو 2014 وأغسطس 2015، وشملت 230 امرأة حامل في طفل مفرد من اللاتي حضرن عيادات ما قبل الولادة في كلية الطب في ولاية كارناتاكا، الهد، على التوالي خلال هذه الفترة. تم قياس ضغط النبض و عمل دوبلر الموجات فوق الصوتية على الشريان الرحمي بين 14-11 أسبوع من الحمل. ويعد ذلك، تمت متابعة هؤلاء النساء الي بعد الولادة لترقب حدوث ارتفاع ضغط الدم لاحقا. النتائج: تم رصد حدوث ارتفاع في ضغط الدم بشكل متكرر إذا كان ضغط النبض مرتفعا (16.0% مقابل 14.4% من حالات الحمل ؛ 20.1% = 9، إذا كان هناك ارتفاع في ضغط الدم (15.1% مقابل 12.5% من حالات المواعدة الترقب حدوث ارتفاع ضغط الدم لاحقا. النتائج: تم رصد حدوث ارتفاع في ضغط الدم بشكل متكرر إذا كان ضغط النبض مرتفعا (16.0% مقابل 14.4% من حالات الحمل ؛ 20.1% = 9، إذا كان هناك ارتفاع في المق (15.1%). (15.1% مقابل 12.5% من حالات الحمل؛ 20.5% مقابل 14.4% من حالات الحمل ؛ 20.1% مناك المناع من حالات الحمل؛ 20.6% (15.1% مقابل 12.5%). من حالات الحمل؛ 20.5% من مؤشر المقاومة IR (22.2% مقابل 15.5% معامل خطورة ارتفاع من عامل عرفة الذه الحصائية بين ارتفاع مؤشر النبض (PI) وارتفاع ضغط الدم (20.0% – 9). وكان معامل خطورة ارتفاع ضغط الدم حوالي سبعة أضعاف أعلى إذا تم استخدام اثنين أو أكثر من مؤشرات مقاومة الشرايين، إلا مع وجود الشق الأنبساطي بالإضافة من عامل المحوصومية (25.5%)، الا في وجود شق انبساطي. وكان لقيمة قطع مؤشر النبض الخاصة. 20.5% ودرجة جيدة من معامل الخصوصية (25.5%)، الا في وجود شق انبساطي. وكان لقيمة قطع مؤشر النبض الخاصة بالسكان في حدود 17.5% من مؤشرات المقاومة الشريين، إلا مع ورتفاع مؤشر النبض من معامل الخصوصية (25.5%)، الا في وجود شق انبساطي. وكان القيمة قطع مؤشر النبض الخاصة بالسكان في حدود 17.5% من من معامل الضري النبض الخاصة بالسكان في حدود 17.5% من من معامل الخاصة بالسكان في وحود قر ورتباع مؤشرات المقاومة الشريين، إلا مع رأدةاع مؤشر النبض العراع في طرا مع مؤشرات مقاومة الشريين (27.5%)، الخرصة وي معام النجض. 25.5% من ما ما الخصومية المربة (25.5%)، الخرصة الفرا مؤشرات ال

الكلمات المفتاحية، مقاومة الأوعية الدموية؛ ضغط النبض؛ الشريان الرحمي؛ دوبلر الموجات فوق الصوتية؛ ارتفاع ضغط الدم الناجم عن الحمل؛ الهند.

Advances in Knowledge

- Among the studied cohort, a raised uterine artery pulsatility index (PI) in the late first trimester was significantly associated with the development of hypertension later in pregnancy.
- Moreover, the risk of subsequently developing hypertension was approximately seven-fold higher if two or more arterial resistance indicators in the late first trimester were used in combination, except with certain combinations of indicators.

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Application to Patient Care

- The findings of the current study indicate that selected indicators of arterial resistance in the late first trimester—including pulse pressure (PP) calculated from routinely recorded blood pressure measurements during regular healthcare visits and uterine artery PI determined via Doppler ultrasonography during nuchal translucency screening—can be used to predict the development of hypertension later in pregnancy.
- However, population-specific reference values for arterial resistance indicators are needed in order to more reliably predict the development of pregnancy-related hypertension among specific patient groups.

URING PREGNANCY, THE DEVELOPMENT of hypertension after 20 gestational weeks is associated with significant maternal and fetal morbidity and mortality.1 Along with sepsis and haemorrhage, it is one of the three main causes of maternal mortality; nearly 15% of deaths are directly due to hypertensive disorders.² As early detection is therefore critical, tests to predict pregnancy-related hypertension have been developed using the following indicators: placental perfusion and vascular resistance (e.g. 'roll-over' and cold pressor tests and uterine artery Doppler evaluations); placental products (e.g. proangiogenic and antiangiogenic proteins, human chorionic gonadotropin, placental protein 13 and inhibin A measurements); renal dysfunction (e.g. fractional urate clearance and microalbuminuria tests); and endothelial dysfunction (e.g. fibronectin, P- and L-selectin and vascular cell adhesion molecule 1 assessments).3 Unfortunately, these investigations and even proteomic and metabolomic tests have all failed individually to provide a reliable means of predicting pregnancy-related hypertension.³ This may be because most of these tests are carried out after 16 gestational weeks, whereas pregnancy-related hypertension by definition manifests after 20 gestational weeks; this would suggest that the disease pathology occurs beforehand, perhaps even during the first trimester of pregnancy.4

Vasospasm is central to the pathology of pregnancy-related hypertension and affects multiple organ systems, including uteroplacental circulation. As such, analysing arterial compliance is thought to be helpful in predicting pregnancy-related hypertension.⁵ Arterial compliance in systemic circulation can be measured via pulse pressure (PP), while compliance in uteroplacental circulation can be gauged using uterine artery Doppler flow studies. Previous research has shown that a 1 mmHg rise in PP during early pregnancy could be associated with a 6% increase in the risk of developing pre-eclampsia.6 Similarly, a study evaluating the uterine artery pulsatility index (PI) demonstrated that there is a greater decrease in uterine artery PI between 11-14 gestational weeks and 21-25 gestational weeks in pregnancies with a normal outcome compared to those with preeclampsia.⁷ The present study aimed to examine the potential association between arterial resistance indicators in the late first trimester, including PP and uterine artery Doppler flow velocimetry indices, and the occurrence of hypertension later in pregnancy.

Methods

This study took place between May 2014 and August 2015 at a medical college in southern Karnataka, India. The inclusion criteria included consecutive women who were between 11-14 gestational weeks with singleton pregnancies attending antenatal units attached to the medical college during the study period. Women with a prior history of pregnancyrelated hypertension, those currently taking drugs likely to interfere with vasculature or circulation (e.g. β-mimetics, aspirin, heparin, vasodilators, smooth muscle relaxants, antioxidants or calcium) and known cases of vascular disease, autoimmune disorders, essential hypertension, renal disease, diabetes mellitus or antiphospholipid syndrome were excluded from the study. The necessary sample size was calculated based on a known incidence of 15% for hypertensive disorders of pregnancy, in order to provide a 95% confidence interval (CI) and with 80% power, according to the following formula:8

$n = Z^2 P(1-P)/d^2$

where Z is the level of confidence (95%), P is the expected prevalence (15%) and d is the desired precision (3–5%). These calculations resulted in a required sample size of 384. Of the 8,043 deliveries by women who underwent antenatal care at the selected antenatal clinics during the study period, pregnancy-related hypertension was present in 1,190 cases (14.8%). There were 504 women who met the inclusion criteria; however, 33 (6.5%) either miscarried or delivered before 32 gestational weeks and 142 (28.2%) did not deliver at the hospital. Therefore, a total of 329 women (65.3%) were included in the final analysis.

At the time of recruitment, each participant's blood pressure (BP) was taken after a 20-minute resting period. The BP measurements were taken from the brachial artery of the non-dominant arm while sitting, using a calibrated mercury sphygmomanometer and a cuff with a length of 1.5 times that of the upper arm circumference.9 The PP was calculated as the difference between systolic and diastolic recordings or the first and fifth Korotkoff sounds.10 As there was no standard reference range available for PP, 100 non-pregnant healthy women between 15-40 years old were recruited among postgraduates, interns, medical students, nursing students and staff nurses at the antenatal units for the purposes of recording their BP. From their BP measurements, the mean PP ± standard deviation of this group was calculated to be 38.33 ± 6.44 mmHg. Therefore, for the pregnant women, PP was considered low if it was less than two standard deviations below this mean (i.e. 25.5 mmHg) and high if it was more than two standard deviations above this value (i.e. 51.0 mmHg).

Transabdominal obstetric ultrasound scans were performed using a HD7 XE ultrasound system (Philips Healthcare, Bothell, Washington, USA) or a Voluson E10 ultrasound system (GE Healthcare, Bangalore, Karnataka, India) equipped with a 3.5-MHz curvilinear transducer. The uterine arteries on each side were localised at the level of the internal opening of the cervix by colour-flow mapping. Pulsed wave Doppler ultrasonography was performed with the sampling gate set at 2 mm to cover the whole vessel. The angle of insonation was maintained at $<50^{\circ}$. The PI and resistive index (RI) and the mean values of the right and left uterine arteries were calculated. For the purposes of the study, the reference upper limit for the indices was based on previously reported 95th centile values of 2.35 and 0.85 for PI and RI, respectively.^{11,12} The presence or absence of a diastolic notch (DN) on both sides was also noted.

To determine the development of hypertension later in pregnancy, the women were followed-up until delivery with routine assessment of BP values at each antenatal visit. Additionally, a final BP measurement for each woman was taken post-delivery just before they were discharged from the hospital. A diagnosis of hypertension was made when BP measurements taken after 20 gestational weeks exceeded 140 mmHg systolic and/or 90 mmHg diastolic on two different occasions and at least four hours apart, with diastolic pressure defined as Korotkoff phase V.13 Throughout the duration of the study, BP and Doppler measurements were made by different investigators using standard protocols.^{14,15} The investigators were not involved in the diagnosis or management of any of the women. Pulsed wave Doppler ultrasound measurements were not revealed to the obstetricians in charge of patient management.

Relative risk (RR) was calculated to determine the probability of participants developing hypertension with the presence of an arterial resistance indicator (high PP, raised PI and RI or the presence of a DN), both alone and in various combinations. Sensitivity, specificity and positive and negative predictive values were calculated for individual Doppler parameters. A receiver-operating curve was plotted for PI and RI to determine cut-off values for this study population. The Statistical Package for the Social Science (SPSS), Version 15.0 (IBM Corp., Chicago, Illinois, USA) was used for data analysis. A *P* value of <0.050 was considered significant.

This study was evaluated by the Departmental and Scientific Committees of Kasturba Medical College, Manipal University, Mangalore, Karnataka, and received approval from the institutional ethics committee (IEC KMC MLR #04-14/98). All women gave written consent before participating in the study.

Results

A total of 329 women were included in the study with a mean age of 24.6 ± 4.2 years. There were 59 women (17.9%) under 20 years old, 144 between 21-25 years old (43.8%), 100 (30.4%) between 26-30 years old and 26 (7.9%) over 30 years old. Of all the women studied, 208 (63.2%) were *primigravidae*. Pregnancy-related hypertension was noted in 48 women (14.6%); of these, 33 women (68.8%) were diagnosed during a prenatal check after 32 gestational weeks, while six (12.5%) were diagnosed between 28-32 gestational weeks. A total of 15 women (31.3%) were diagnosed while in labour during admission to the hospital; however, their BP reverted to normal within 48 hours of delivery. There were 38 babies (11.6%) born weighing less than 2.5 kg.

With regards to arterial resistance indicators, 17 women (5.2%) had high PP, 251 (76.3%) had a DN present, five (1.5%) had a raised PI and nine (2.7%) had a raised RI. Hypertension was more likely to occur with high PP (17.6% versus 14.4% of pregnancies without high PP; P = 0.713). Similarly, hypertension was more frequent with the presence of a DN (15.1% versus 12.8% without a DN; P = 0.612) and with a raised RI (22.2% versus 14.3% without raised RI; P = 0.366). There was a significant association between raised PI and the development of hypertension (80.0% versus 13.6% without raised PI; P = 0.013) [Table 1]. PI was found to have positive and negative likelihood ratios of 20.7 and 0.9, respectively.

A combination of different arterial resistance indicators were tested in order to find an accurate predictor of pregnancy-related hypertension. Women **Table 1:** Associations between arterial resistanceindicators and pregnancy-related hypertension amongpregnant women between 11-14 gestational weeksattending antenatal units in Karnataka, India (N = 329)

Indicator	Total,	Hypertensive patients		
	n (%)	n (%)	P value	
Pulse pressure				
High*	17 (5.2)	3 (17.6)	0.713	
Not high	312 (94.8)	45 (14.4)		
Diastolic notch				
Present	251 (76.3)	38 (15.1)	0.612	
Absent	78 (23.7)	10 (12.8)	0.612	
Pulsatility index				
$Raised^\dagger$	5 (1.5)	4 (80.0)	0.013	
Not raised	324 (98.5)	44 (13.6)	0.015	
Resistive index				
Raised [‡]	9 (2.7)	2 (22.2)	0.266	
Not raised	320 (97.3)	46 (14.4)	0.300	

*Pulse pressure of ${\geq}51.0$ mmHg. [†]Pulsatility index of ${\geq}2.35.^{11}$ [‡]Resistive index of ${\geq}0.85.^{12}$

Table 2: Relative risk of pregnancy-related hypertensionaccording to arterial resistance indicators alone orin combination among pregnant women between11-14 gestational weeks attending antenatal units inKarnataka, India (N = 329)

Total, n	Hypertensive patients		
(%)	n (%)	RR (95% CI)	
17 (5.2)	3 (17.6)	1 22 (0 42 2 22)	
312 (94.8)	45 (14.4)	1.22 (0.42-5.55)	
251 (76.3)	38 (15.1)	1 17 (0 61 - 2 25)	
78 (23.7)	10 (12.8)	1.17 (0.01-2.23)	
5 (1.5)	4 (80.0)	5 90 (3 51-9 88)	
324 (98.5)	44 (13.6)	0.00 (0.01 0.00)	
9 (2.7)	2 (22.2)	1 55 (0 44–5 40)	
320 (97.3)	46 (14.4)	1.55 (0.11 5.10)	
2 (0.6)	2 (100.0)	7 10 (5 42 0 20)	
327 (99.4)	46 (14.1)	7.10 (5.45-9.29)	
	Total, n 17 (5.2) 312 (94.8) 251 (76.3) 78 (23.7) 5 (1.5) 324 (98.5) 9 (2.7) 320 (97.3) 2 (0.6) 327 (99.4)	Total, n (%) Hyperter n (%) n (%) n (%) 17 (5.2) 3 (17.6) 312 (94.8) 45 (14.4) 312 (94.8) 45 (14.4) 251 (76.3) 38 (15.1) 78 (23.7) 10 (12.8) 78 (23.7) 10 (12.8) 324 (98.5) 44 (13.6) 9 (2.7) 2 (22.2) 320 (97.3) 46 (14.4) 2 (0.6) 2 (100.0) 327 (99.4) 46 (14.1)	

PI + DN				
Abnormal	4 (1.2)	4 (100.0)	7.20(5.61, 0.72)	
Normal	325 (98.8)	44 (13.5)	7.50 (5.01-9.72)	
PI + PP				
Abnormal	1 (0.3)	1 (100.0)	6 00 (5 25 0 00)	
Normal	328 (99.7)	47 (14.3)	0.90 (5.55-9.09)	
PI + RI + DN				
Abnormal	2 (0.6)	2 (100.0)	7 10 (5 42 0 20)	
Normal	327 (99.4)	46 (14.1)	7.10 (5.45-9.29)	
PI + RI + PP				
Abnormal	1 (0.3)	1 (100.0)	6 00 (5 25 0 00)	
Normal	328 (99.7)	47 (14.3)	0.90 (5.55–9.09)	
PI + DN + PP				
Abnormal	1 (0.3)	1 (100.0)	6 00 (5 25 0 00)	
Normal	328 (99.7)	47 (14.3)	0.90 (5.55–9.09)	
RI + PP				
Abnormal	1 (0.3)	1 (100.0)	6 90 (5 35 9 09)	
Normal	328 (99.7)	47 (14.3)	0.90 (3.33-9.09)	
RI + DN				
Abnormal	7 (2.1)	2 (28.6)	1.00 (0.6 .6.65)	
Normal	322 (97.9)	46 (14.3)	1.99 (0.0-0.05)	
DN + PP				
Abnormal	13 (4.0)	4 (30.8)	2 20 (0 02 E 22)	
Normal	316 (96.0)	44 (13.9)	2.20 (0.95–5.22)	
RI + PP + DN				
Abnormal	1 (0.3)	1 (100.0)	6 00 (5 25 0 00)	
Normal	328 (99.7)	47 (14.3)	6.90 (5.35–9.09)	
PI + RI + DN + PP				
Abnormal	1 (0.3)	1 (100.0)	6.90 (5.35–9.09)	
Normal	328 (99.7)	47 (14.3)		

RR = relative risk; CI = confidence interval; PI = pulsatility index; RI = resistive index; DN = diastolic notch; PP = pulse pressure. *Pulse pressure of \geq 51.0 mmHg. [†]Pulsatility index of \geq 2.35.¹¹ [‡]Resistive index of \geq 0.85.¹²

with any combination of at least two indicators had an approximately seven-fold higher risk of developing hypertension than those without these indicators. However, this did not include two combinations—the presence of DN and a raised RI or the presence of DN and high PP—which resulted in a RR of 1.99 and 2.20, respectively. On its own, raised RI did not appear to be a predictor of hypertension (RR = 1.55; 95% CI: 0.44–5.40); however, it augmented RR values for PP

Table 3: Validation measures of arterial resistanceindicators as predictors of pregnancy-relatedhypertension

Validation measure	Indicator			
	PI	RI	DN	PP
Sensitivity, %	8.3	4.2	79.2	6.3
Specificity, %	99.6	97.5	24.2	95.0
PPV, %	80.0	22.2	15.1	17.6
NPV, %	86.4	85.6	87.2	85.6

PI = pulsatility index; *RI* = resistive index; *DN* = diastolic notch;

PP = *pulse pressure; PPV* = *positive predictive value; NPV* = *negative predictive value.*

(RR = 6.90; 95% CI: 5.35–9.09 in combination versus RR = 1.22; 95% CI: 0.42–3.33 alone) and, to some extent, for PI as well (RR = 7.10; 95% CI: 5.43–9.29 in combination versus RR = 5.90; 95% CI: 3.51–9.88 alone). The presence of a DN alone did not help with risk identification (RR = 1.17; 95% CI: 0.61–2.25); however, in certain combinations with other indicators, the RR increased (6.9–7.3) [Table 2].

In terms of validation of the indicators as predictors of pregnancy-related hypertension, only the presence of a DN showed good sensitivity (79.2%); the negative predictive value of this indicator was also high (87.2%), although specificity (24.2%) and positive predictive value (15.1%) were very poor. Raised PI, which had shown an association with hypertension, failed to be a sensitive marker (8.3%); however, it had good specificity (99.6%), a positive predictive value of 80.0% and a negative predictive value of 86.4%. As indicators, both RI and PP demonstrated poor sensitivity (4.2% and 6.3%, respectively), but had high specificity (97.5% and 95.0%, respectively) and negative predictive values (85.6% each) [Table 3].

In order to find specific reference levels for the study population, a receiver-operating curve was applied to the data. A cut-off value of 1.72 was obtained for PI, with increased sensitivity (8.3% versus 70.8%) and without a substantial decrease in specificity (99.6% versus 65.1%). [Table 4]. It was not possible to derive a population-specific cut-off value for RI.

Discussion

In the current study, the incidence of pregnancyrelated hypertension (14.6%) mirrored the incidence noted in previous years at the same facility, based on an analysis of unpublished statistics. Alarmingly, this rate was almost 2.1-times higher than the global estimate (6–8%) published by the National High Blood Pressure Education Program working group.¹⁶ However, of the women with hypertension in the present study, almost Table 4: Comparison of reference and population-specific pulsatility index cut-off values to predict pregnancy-related hypertension among pregnant women between 11–14 gestational weeks attending antenatal units in Karnataka, India (N = 329)

Validation measure	Cut-off value			
	2.35*		1.72	
	HTN	No HTN	HTN	No HTN
Positive tests	4	1	34	98
Negative tests	44	280	14	183
Sensitivity, %	8.3		70.8	
Specificity, %	99.6		65.1	
PPV, %	80.0		25.8	
NPV, %	86.4		92.8	

HTN = *hypertension; PPV* = *positive predictive value; NPV* = *negative predictive value.*

*Reference value sourced from Martin M, Bindra R, Curcio P, Cisero S, Nicolaides KH. Screening for pre-eclampsia and fetal growth restriction by uterine artery Doppler at 11–14 weeks of gestation.¹¹

a third were diagnosed during labour; it is possible that the rise in BP observed in these women was temporary since pregnancy endothelin-1 concentrations significantly increase during labour, especially with a vaginal delivery.^{17,18} Therefore, if these cases were to be excluded, the incidence would fall to 10.0% (n = 33), which is comparable to previously published hospital-based incidence/prevalence rates.¹⁹ It should also be noted that most classifications of pregnancyrelated hypertension exclude pressure recordings taken during labour.²⁰

In general, PP is considered a surrogate measurement of vascular compliance.21 Thadhani et al. reported significantly higher PP values at 7-15 gestational weeks among women who subsequently developed pre-eclampsia.6 This finding is similar to that of the present study, which found that women with high PP values at 11-14 gestational weeks more frequently developed hypertension later during their pregnancy. Increased turbulence, resistance to flow and the presence of a DN have also been associated with the subsequent development of pregnancyrelated hypertension.²² In the present study, there was a marginally higher occurrence of pregnancy-related hypertension among patients with a DN; moreover, while the presence of a DN alone did not help with risk identification, its presence in combination with high PP or a raised PI increased the likelihood of hypertension occurring. This indicator demonstrated good sensitivity and negative predictive value, indicating that the absence of a DN late in the first

trimester reduced the likelihood of subsequent pregnancy-related hypertension. On its own, raised RI was also not useful as a predictor of hypertension, yet the risk of hypertension increased when this indicator was combined with PP and, to some extent, PI.

Raised PI was significantly associated with hypertension in the current study. These findings are in agreement with those of Plasencia et al., in which a steep decrease in uterine artery PI between 11-13.6 and 21-24.6 gestational weeks was noted among normal pregnancies in comparison to those which developed pre-eclampsia.7 In a previous study, the researchers concluded that maternal variables together with uterine artery PI in the first trimester provided a sensitive predictor of pre-eclampsia, especially of severe early-onset disease.23 Similarly, Martin et al. found that screening for pre-eclampsia at 11-14 gestational weeks with uterine artery Doppler parameters allowed the identification of a high proportion of severe pre-eclampsia and/or fetal growth restriction cases.11 Nevertheless, although the findings from this study agree with earlier studies in part, the authors of the current study believe that the effect of uterine artery impedance is not uniform. Due to their low predictive value, Sciscione et al. do not recommend uterine artery Doppler testing in either high- or low-risk pregnancies.²⁴ As this screening technique is not standardised or universally used, the criteria for abnormal values have yet to be determined.²⁵ There was wide variation in the findings of the current study when different cut-off values for pulse wave analysis were used; this was thought to be mainly attributable to the use of cut-off values for PI and RI sourced from previous studies.11,12 Indeed, calculations of cut-off values in the current study indicated that these were lower for the studied Indian population than the reference values for other populations.^{11,12} Therefore, the results of the current study would be more comparable if the cut-off values had been specific to the study population.

The current study is subject to a few limitations. First, the findings are based on a small number of observations and the study included women who developed hypertension during labour and late in their pregnancies. Second, there were possible interobserver variations in the recording of BP and Doppler flow measurements; however, it was not possible to have a single person record all of the measurements. Moreover, inter-observer variations were believed to be minimal as the antenatal care facilities attended by the patients follow a checklist for recording BP and Doppler ultrasonography was performed by consultant radiologist-sonologists following a uniform protocol with computer-generated Doppler flow values. Third, there were very few cases with abnormal Doppler flow values at the end of the study, especially when combinations of PP, DN, PI and RI were used. This drawback could be overcome in future studies involving a greater number of cases. In contrast, the strengths of this study include the development of a cut-off PI value for a local Indian population. Furthermore, there is an urgent need for a reliable and early indicator of pregnancy-related hypertension. Currently, there are no accepted tests for predicting the occurrence of hypertension during pregnancy. A simple, non-invasive and inexpensive test-such as PP as one of the indicators of arterial resistance-may be of great help to primary care physicians at remote facilities in order to prioritise care, make early referrals and provide appropriate counselling for pregnant women.

Conclusion

Uterine artery PI in the late first trimester was significantly associated with the subsequent development of hypertension later in pregnancy. Additionally, the use of a combination of arterial resistance indicators increased prediction of the subsequent development of hypertension. The authors suggest that future studies develop population-specific reference cut-off values for PI and RI.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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