

STUDY OF FIRST TRIMESTER UTERINE ARTERY DOPPLER AND SERUM CALCIUM IN PREDICTION OF HYPERTENSIVE DISORDERS OF THE PREGNANCY

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Abstract

Background: Hypertensive disorders in pregnancy, affecting 5-10% of pregnancies, are a leading cause of maternal mortality and morbidity, with preeclampsia posing serious risks to both the mother and foetus and long-term health impacts. This study evaluated first-trimester uterine artery Doppler screening and serum calcium levels to predict and associate them with preeclampsia risk. **Material and Methods:** This prospective quantitative experimental study was conducted on 386 pregnant women at the Department of Obstetrics and Gynaecology-OPD, Govt Villupuram Medical College and Hospital, Mundiambakkam, Tamil Nadu. A thorough history and clinical examinations, including BMI, blood pressure, and proteinuria, were conducted at each visit, with ultrasound scans at 11–13 weeks, and routine haematological and serum calcium levels were noted. The protein levels were measured using dipstick reagent strips with bromophenol blue. **Results:** Among the patients with GHTN, 92.85% had serum calcium levels below 8.6, and 71% of the newborns had a birth weight < 2.5 kg. In preeclampsia patients, 88% had serum calcium levels < 8.6, and 52% of newborns had a birth weight < 2.5 kg. Serum calcium levels were below 8.6 in 88% of the cases, with 72% delivering preterm, 48% undergoing LSCS, and 52% having vaginal deliveries. Among the GHTN patients, 42.85% had changes in the left uterine artery and 71.42% had changes in the right uterine artery, with an average of 71.42%. **Conclusion:** Early and cost-effective detection of preeclampsia through first-trimester uterine artery Doppler and identification of high-risk factors are crucial for preventing complications and improving maternal and foetal outcomes.

INTRODUCTION

Hypertensive disorders in pregnancy affect 5-10% of all pregnancies and represent the most common medical complication of pregnancy. According to the World Health Organization's systemic review of maternal mortality worldwide, hypertension remains a leading cause of maternal mortality. Hypertensive disorders are responsible for not only maternal death, but also substantial morbidity in pregnant women. The long-term impact of hypertension in pregnancy in the form of chronic hypertension and increased lifetime cardiovascular risk is also present. Preeclampsia is a multisystem illness that, when it manifests, presents a serious risk to both the mother and the foetus. Preeclampsia can cause significant

perinatal and maternal morbidity on its own, aside from its most severe consequence of developing into eclampsia.^[1,2]

Preeclampsia, eclampsia, gestational hypertension, chronic hypertension with or without superimposed pre-eclampsia/eclampsia, and other hypertensive diseases of pregnancy all carry a considerable risk of morbidity.^[3,4] According to the American College of Obstetricians and Gynaecologists, hypertension in pregnancy is defined as systolic blood pressure (SBP) > 140 mmHg or higher and diastolic blood pressure (DBP) > 90 mmHg or higher (Korotkoff V). Maternal, foetal, and neonatal morbidities and deaths are frequently caused by hypertensive disorders of pregnancy. Abruption placentae, cerebrovascular events, organ failure, and

disseminated intravascular coagulation are all more common in women with severe preeclampsia. Preeclampsia women are more likely to have intrauterine growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome (RDS), admission to neonatal intensive care, cerebral palsy and intrauterine mortality.^[5]

Between 5% and 10% of all pregnancies are complicated by hypertension. Two to eight percent of all pregnancies worldwide are complicated by preeclampsia. Due to changes in maternal demographics, such as growing maternal age and higher pre-pregnancy weight, the prevalence of hypertension is rising. Eclampsia, however, has decreased as a result of better prenatal care and a rise in the use of antenatal therapies, such as magnesium sulphate prophylaxis and blood pressure control, as well as timely delivery through labour induction or caesarean section, which serve as a treatment for pre-eclampsia/eclampsia.^[6,7]

By the eighth week, trophoblasts typically begin to infiltrate the decidual part of the spiral arteries, and by the twelfth week, this invasion is typically completed. Subsequently, the second stage of spiral artery invasion begins, during which trophoblasts similarly invade the myometrial part of the spiral arteries. The spiral artery bed does not undergo this transition in the vast majority of preeclamptics, increasing flow resistance into the intervillous area. Uterine artery waveform is the preferred approach for inferentially monitoring the condition of the spiral artery bed. Doppler ultrasonography measurements of increased uterine artery velocimetry in the early and middle trimesters should give indirect evidence of this process and act as a screening tool for preeclampsia.^[8,9]

Aim

This study evaluated first-trimester uterine artery Doppler screening and serum calcium levels to predict and associate them with preeclampsia risk.

MATERIALS AND METHODS

This prospective quantitative experimental study was conducted on 386 pregnant women at the Department of Obstetrics and Gynaecology-OPD, Govt Villupuram Medical College and Hospital, Mundiyaikkam, and Tamil Nadu from 2021-2022. The study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

All mothers with AN attending antenatal checkup at a gestational age of 11–13 weeks were included.

Exclusion Criteria

Patients with twin gestation, chronic hypertension, major foetal anomalies incompatible with life, past h/o preeclampsia, missed abortion, conception by in vitro fertilization, and diabetes mellitus type 2 were excluded.

Methods

After obtaining written informed consent from the pregnant women willing to participate in the study, preliminary data were collected. Thorough history to determine patient demographics, gestational age, and risk factors associated with pregnancy. BMI was calculated, and blood pressure was recorded in the sitting position after 10 min of rest, and the reading was repeated above 140/90 mmHg after 4 h. The protein portion of the dipstick reagent strip measures the protein based on the protein error of the PH dye indicator, principle (method) using bromophenol blue. Development of the colour range from yellow for negative through yellow green and green to green blue for a positive reaction. Routine haematological investigations and serum calcium levels were also noted. Clinical examination was performed at each visit, along with weight gain, blood pressure, and proteinuria. Ultrasound scans were performed at 11–13 weeks and 6 days. Physical and systemic examinations were also performed.

Statistical Analysis

The data were coded and entered into a computer using Microsoft Excel. The analysis was performed using SPSS software. Statistical tests were employed, including descriptive statistics, chi-square test, and Fisher's exact test, which were used whenever the data were presented in terms of frequency, and Student's t-test was used to test significance when the results were presented as mean \pm standard deviation (SD). Statistical significance was set at $P < 0.05$. IBM SPSS version 22 was used for the statistical analysis.

RESULTS

The previous obstetric history showed that 320 (83.11%) patients had no notable issues, while 44 (11.43%) had a lower segment caesarean section. Regarding family history, 331 (85.97%) patients reported no significant conditions, whereas 48 (12.47%) had hypertension. Among other medical histories, 276 (71.50%) had no significant issues; however, 35 (9.06%) had gestational diabetes mellitus on a meal plan. Gestational age at delivery was the most common at 38 weeks (137, 35.58%), followed by 40 weeks (57, 14.81%). The majority of gestational ages at the time of assessment were between 12 weeks and 1 to 6 days (276, 71.69%). [Table 1]

The highest obstetric score was for primigravida (PRIMI) 216 (56.11%). Intrauterine growth retardation was observed in 301 (77.97%) patients. Oligohydramnios was observed in 347 patients (77.97%). Gestational hypertension and preeclampsia were present in 372 (96.37%) and 361 (93.76%) of the patients, respectively. Eclampsia and HELLP syndrome were absent in all the patients (0%). The mode of delivery was predominantly

normal vaginal delivery 171 (44.94%), followed by emergency LSCS 68 (17.66%). [Table 2]

Among the patients with gestational hypertension (GHTN), 92.85% had serum calcium levels < 8.6, and 71% of the newborns had a birth weight < 2.5 kg. Among preeclampsia patients, 88% had serum calcium levels < 8.6, and 52% of newborns had a birth weight < 2.5 kg. [Table 3]

Among preeclampsia patients, 76% were primiparous, 24% had a family history, 72% had changes in the left uterine artery, and 52% in the right uterine artery, with an average of 60%. Aspirin intake was noted in 68%, intrauterine growth restriction (IUGR) in 36%, and oligohydramnios in 40% of patients. Serum calcium levels were below 8.6 in 88% of the cases, with 72% delivering preterm, 48% undergoing LSCS, and 52% having vaginal deliveries. The birth weight was < 2.5 kg in 52% of cases. Among the patients with GHTN, 42.85% had changes in the left uterine artery and

71.42% had changes in the right uterine artery, with an average of 71.42%. [Table 4]

In the study population, 11.65% were taking aspirin, while 88.34% were not. Among the preeclampsia patients, the same distribution was applied. Regarding the Doppler results, 89.61% had normal findings, with 3.64% showing a left uterine diastolic notch and 2.60% showing a right uterine diastolic notch. Absent diastolic flow was observed in 1.04% of the multiple Doppler examinations, and anomalous foetuses were noted in 1.82% of the patients. Anti-phospholipid antibody syndrome was present in 1.55%, absent in 3.86%, and not tested in 94.80% of the patients. [Table 5]

The mean age of the study population was 25.72 ± 3.84 years. Uterine artery measurements averaged 1.93 ± 0.72 on the left and 2.02 ± 0.75 on the right, with an overall average of 1.96 ± 0.6, respectively. The mean serum calcium level was 9.01 ± 0.44, and the mean birth weight was 2.84 ± 0.51 kg. [Table 6]

Table 1: Demographic details

		Frequency (%)
Previous obstetric history	Neonatal death	10 (2.59%)
	Bad obstetric history, Rheumatic heart disease	2 (0.52%)
	Intrauterine death	7 (1.81%)
	Lower segment caesarean section	44 (11.43%)
	Molar pg	2 (0.52%)
	Nil	320 (83.11%)
Family history	Diabetes mellitus	4 (1.04%)
	Hypertension and diabetes mellitus	2 (0.52%)
	Hypertension	48 (12.47%)
	Nil	331 (85.97%)
Other medical history	Absent	276 (71.50%)
	Quit	33 (8.54%)
	Asthma	2 (0.51%)
	Gestational diabetes mellitus on meal plan	35 (9.06%)
	GDM on OHA	10 (2.59%)
	Hypothyroidism	10 (2.59%)
	S.VSD	2 (0.51%)
Gestational age at delivery	33	5 (1.30%)
	34	10 (2.60%)
	35	8 (2.08%)
	36	22 (5.71%)
	37	38 (9.87%)
	38	137 (35.58%)
	39	54 (14.03%)
	40	57 (14.81%)
	QUIT	54 (14.03%)
Gestational age	11 weeks 1 day to 6 days	46 (11.95%)
	12 weeks 1 day to 6 days	276 (71.69%)
	13 weeks	109 (16.36%)

Table 2: Various parameters of the patients

		Frequency (%)
Obstetrics score	G3P2L0	2 (0.52%)
	G2A1	23 (5.97%)
	G2P1L0	5 (1.30%)
	G2P1L1	77 (20.00%)
	G2P1L2	6 (1.56%)
	G3A2	2 (0.52%)
	G3P1L1A1	33 (8.57%)
	G3P2L2	5 (1.30%)
	G4P1L1A2	2 (0.52%)
	G4P2L1A1	4 (1.04%)
	G5P2L1A2	2 (0.52%)
	G5P1L1A3	2 (0.52%)
	G6P2L0A3	6 (1.56%)

	PRIMI	216 (56.11%)
Intrauterine growth retardation	Present	301 (77.97%)
	Absent	85 (77.97%)
Oligohydramnios	Present	347 (77.97%)
	Absent	39 (77.97%)
Gestational hypertension	Present	372 (96.37%)
	Absent	14 (3.626%)
Preeclampsia	Present	361 (93.76%)
	Absent	25 (6.47%)
Eclampsia	Present	0
	Absent	386 (100%)
HELLP	Present	0
	Absent	386 (100%)
Mode of delivery	Elective - LSCS	38 (9.87%)
	Emergency - LSCS	68 (17.66%)
	FAVD	2 (0.52%)
	Normal vaginal delivery	171 (44.94%)
	QUIT	56 (14.03%)
	Vacuum assisted vaginal delivery	50 (12.99%)

Table 3: S. Calcium, birth weight of GHTN and pre-eclampsia patients

		Percentage
S. calcium (GHTN)	<8.6	92.85%
	>8.6	7.15%
Birth weight (GHTN) (kg)	<2.5	71%
	>2.5	29%
S. calcium (Preeclampsia)	<8.6	88%
	>8.6	12%
Birth weight (Preeclampsia) (kg)	<2.5	52%
	>2.5	48%

Table 4: Various clinical parameters of pre-eclampsia and GHTN patients

		Percentage
Various parameters among pre-eclampsia patients	PARITY - PRIMI	76%
	G2A1	8%
	G2P1L1	8%
	G3P2L2	8%
	PRE OB H/O	0
	FAMIL H/O	24%
	U/A LEFT	72%
	U/A RT	52%
	AVERAGE	60%
	ASP INTAKE	68%
	IUGR	36%
	OLIGO	40%
	OBS MED H/O	0%
	S.CAL	88%
	GA TERM	28%
	GA PRETERM	72%
Uterine artery doppler changes among GHTN patients	LSCS	48%
	VD	52%
	<2.5Kg	52%
Uterine artery doppler changes among pre-eclampsia patients	>2.5 Kg	48%
	U/A LEFT	42.85%
	U/A RT	71.42%
	AVERAGE	71.42%
Uterine artery doppler changes among pre-eclampsia patients	UT ART LT	72%
	UT ART RT	52%
	AVERAGE	60%

Table 5: Descriptive analysis of doppler and other parameters

		Frequency (%)
Aspirin (study population)	Yes	45 (11.65%)
	No	341 (88.34%)
Aspirin (pre-eclampsia population)	Yes	45 (11.65%)
	No	341 (88.34%)
2 - Doppler	Bilateral uterine artery notch+	2 (0.52%)
	Left uterine diastolic notch present	14 (3.64%)
	Normal	345 (89.61%)
	QUIT	14 (3.64%)
	Right uterine diastolic notch present	10 (2.60%)

3 - Doppler	Absent diastolic flow	4 (1.04%)
	Anomalous foetus	7 (1.82%)
	Nil	364 (94.54%)
	QUIT	10 (2.60%)
Anti-phospholipid antibody syndrome	Absent	15 (3.86%)
	Present	6 (1.55%)
	Not done	365 (94.80%)
4 - Doppler	Absent diastolic flow	4 (1.04%)
	Anomalous foetus	7(1.82%)
	Nil	364 (94.54%)
	QUIT	10 (2.60%)
5 - Doppler	Absent diastolic flow	4 (1.04%)
	Anomalous foetus	7 (1.82%)
	Nil	364 (94.54%)
	QUIT	10 (2.60%)
6 - Doppler	Absent diastolic flow	4 (1.04%)
	Anomalous foetus	7 (1.82%)
	Nil	364 (94.54%)
	QUIT	10 (2.60%)

Table 6: Mean values of various parameters

	Mean ± SD
Age	25.72 ± 3.84
Uterine artery(L)	1.93 ± 0.72
Uterine artery (R)	2.02 ± 0.75
Average uterine artery	1.96 ± 0.6
Serum calcium	9.01 ± 0.44
Birth weight	2.84 ± 0.51

DISCUSSION

In our study, 10% of the population developed hypertension, with 6.4% having preeclampsia and 3.6% having gestational hypertension. The mean age was 25.72 ± 3.84 years. Obstetric history showed that 11.43% had a lower segment caesarean section, 2.59% had neonatal death, and 1.81% had intrauterine death. The family history indicated that 12.47% had hypertension, 0.52% had both hypertension and diabetes, and 1.04% had diabetes. The gestational age distribution was 71.69% at 12 weeks and 1-6 days, 16.36% at 13 weeks, and 11.95% at 11 weeks and 1-6 days. Among the study population, 3.64% had a left uterine diastolic notch, 2.60% had a right uterine diastolic notch on 2-Doppler, 1.04% had absent diastolic flow, and 1.82% had an anomalous foetus on 3-Doppler. Oligohydramnios occurred in 39% of participants, with 35.71% of those with gestational hypertension. Intrauterine Growth Restriction (IUGR) was present in 22% of patients, with 64.28% of hypertensive patients delivering IUGR babies.

In a systematic review conducted by Khong et al., uterine artery Doppler velocimetry and unfavourable pregnancy outcomes were compared using various measurement methods and impedance indices. Overall, early onset preeclampsia can be predicted more accurately than late-onset preeclampsia by using first-trimester Doppler interrogation of the uterine artery. Its sensitivity in predicting preeclampsia and foetal growth restriction in low-risk pregnant women is limited to 40–70%, making it an isolated sign of future illness. The first-trimester uterine artery pulsatility index, maternal traits, and biochemical indicators may all be used in

multiparametric prediction models to reach a diagnosis rate of over 90% for early-onset preeclampsia.^[10]

Demers et al. conducted a prospective cohort study of nulliparous women who give birth to a single child at 11 to 13 weeks. With a 10% false-positive rate, UtA-PI, in combination with maternal factors, may predict 45% of preterm PE cases. In conclusion, when gestational age is between 11 and 13 weeks, first-trimester UtA-PI declines and is linked to a higher risk of preterm but not term PE.^[11] In the study by Mohieldein et al., 92.85% of the study population had calcium levels < 8.6, and 7.15% had calcium levels > 8.6. According to the results, normal pregnant women had a blood calcium level of 9.04 mg/dl, whereas the hypertensive disorder in pregnant women S. calcium was 8.38 mg/dl on average (SD). According to this statement, PIH may occur because of low maternal total calcium levels. Therefore, pregnant women should be advised to consume calcium.^[12]

In a study by Demers et al., the mean uterine artery PI was 2.2, similar to that in our study which was 1.96.^[13] In another study by Gomez et al., the mean uterine artery PI was 1.96 in the 11th week, 1.83 in the 12th week, 1.71 in the 13th week, 1.58 in the 14th week which is similar to our study.^[14]

CONCLUSION

Preeclampsia is a life-threatening disorder during pregnancy. Early detection of the disease at a low cost is of utmost importance. The predictive accuracy of first-trimester uterine artery Doppler is superior to that of late-onset disease for the early identification of preeclampsia and foetal growth

retardation. Identification of high-risk factors, screening, and surveillance are of utmost importance in predicting preeclampsia. Preventive therapy, if initiated early on the basis of these screening tests, will help save antenatal women from complications of preeclampsia. Further studies should be conducted to determine temporal associations.

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