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Role Of First Trimistric Uterine Artery Doppler And Maternal Serum Beta Human Chorionic Gonadotropin In Prediction Of Preeclampsia

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ORIGINAL ARTICLE

Role of First Trimistric Uterine Artery Doppler and Maternal Serum Beta Human Chorionic Gonadotropin in Prediction of Preeclampsia

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Abstract

Background: **Despite early acclimation, there is an imbalance in systemic circulation and vasoactive factors. Failure of trophoblast invasion owing to risk, genetic polymorphism, and other factors inhibits the physiological remodeling of spiral arteriolar walls. Doppler demonstrates hemodynamic changes associated with PE. Ultrasound detects 75 % of instances of preterm preeclampsia (PE). In PE, pulsatility index, resistance index, and early diastolic notch (EDN) indicate a maternal vascular disease. Failure of trophoblast invasion is caused by a persistent early diastolic notch or uneven blood flow velocity. vascular endothelial growth factors (VEGFs) influence the placental development of Human Chorionic Gonadotropin (HCG). Signs of PE include high or low HCG levels.**

Aim: **To assess the role of first Trimistric Uterine Artery Doppler and maternal Serum Beta Human Chorionic Gonadotropin (β-HCG) in the prediction of PE.**

Patients and methods: **One hundred pregnant women participated in this prospective observational study at Al-Hussien University Hospital between May 2021 and October 2021.**

Results: **Comparison of urine protein mg/day in the first and second trimesters and relation among cases who developed PE with Uterine artery Doppler indices in the first trimester showed statistically significant differences between study groups for validity (AUC, sensitivity, specificity). High pulsatility index and resistance index in the mother's uterine artery, as well as low β-HCG levels in the first trimester, were associated with PE.**

Keywords: Human chorionic gonadotropin, Preeclampsia, Uterine artery doppler

1. Introduction

Preeclampsia (PE) is defined by proteinuria (≥300 mg/24 h or protein to creatinine ratio greater than 30 mg/mmol or ≥2+ on dipstick testing) and new-onset hypertension (blood pressure ≥140 mmHg systolic or 90 mmHg diastolic) at greater than or equal to 20 weeks' gestation. Patients without proteinuria who show symptoms of renal, hepatic, or hematological dysfunction are now included in the updated criteria from the International Society for the Study of Hypertension and the American College of Obstetricians and Gynecologists. The main reason for of maternal and fetal morbidity and mortality globally is perinatal infection PE. Three to five% of all pregnant women are affected by this, making it the most prevalent medical issue.[1]

Placental dysfunction is a primary cause of PE because it sets off a cascade of pathophysiological alterations. A temporary adaptive reaction takes place, but thereafter the systemic circulation and the vasoactive chemicals become unbalanced. Physiological remodeling of the walls of the spiral arteries is thought to be avoided by a confluence of risk exposure, polymorphic genes, and other factors

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(including vasoactive and vascular remodeling proteins, thrombophilia, hypo fibrinolysis, oxidative stress, lipid metabolism, endothelial injury, and immunogenetic factors).[2] These hemodynamic changes, present before the onset of PE symptoms, can be detected by Doppler testing. Ultrasound's ability to quantitatively and qualitatively evaluate vascular flows has been found to be reliable and reproducible as part of a multimodal ensemble of screening indicators, recognizing 75 % of cases of preterm (before 37 weeks of gestation) pregnancy. PE.[3]

The uterine artery has been extensively examined in PE, and it has been found that the presence of a pulsatility index (PI), RI, and early diastolic notch all indicate the vascular health of the mother. There is evidence linking impaired trophoblast invasion to a persistent early diastolic notch or anomalies in blood flow velocity.[4]

Production of progesterone, implantation, uterine development, and immune cell activity are all regulated by Human Chorionic Gonadotropin (HCG), a pregnancy-specific hormone generated by trophoblast cells (Cole LA, 2010). HCG regulates placental development, angiogenesis and vasculogenesis in addition to vascular endothelial growth factors (VEGFs). Clinical manifestation of PE has been linked to HCG levels, both high and low, according to several research.[5]

This study set out to determine how well Uterine Artery Doppler and maternal Serum Beta Human Chorionic Gonadotropin (β-HCG) could predict the onset of PE in the first trimester.

2. Patients and methods

This prospective observational research was done at Al-Hussien university hospital during the period from May 2021 to October 2021 including 100 pregnant women.

Inclusion criteria: 100 pregnant women who fulfilled the following criteria were included in the study: age group (17–45) years, Gestational age from 11 to 13 weeks, Prim gravida, and single or multiple living gestation.

Exclusion criteria: Pregnant women greater than 13 weeks of gestation, Uncertain gestational age, pelvic pathology as uterine fibroid and intrauterine fetal death, fetal anomalies.

Method All women had their histories, menstrual cycles, pregnancies, and delivery experiences recorded, as well as physicals that included a pelvic, abdominal, and vulvar exam.

Investigations: Routine investigations include complete blood count, blood group, Rh. group, urine analysis, fasting blood sugar and 2 h post-prandial blood sugar, Ultrasounds scan to assess the gestational age and to detect any abnormality, Uterine artery doppler at 11–13 weeks and serum β-HCG level at 11–13 weeks.

2.1. Interventions

Transabdominal ultrasound technique: a 3.5–5 MHz curvilinear transabdominal transducer was used. A midsagittal section of the uterus and cervical canal was obtained, and the transducer is moved laterally until the paracervical vessels were visualized. Color-flow Doppler was applied.

Transvaginal ultrasound technique: a 4.6–8 MHz transvaginal transducer was used. The transducer was placed in the anterior vaginal fornix, and a sagittal section of the cervix was obtained. The vaginal probe was then moved laterally until the paracervical vascular plexus is seen. Color-flow Doppler was applied, and the UA was identified at the level of the cervicocorporeal junction. Measurements were taken at this point before the UA branches into the arcuate arteries.

Ultrasound device model was: Logiq P5.

Code number was: opc_2d.3d_1.

2.2. Sample size

This study base on study carried out by Emine *et al*. was used to calculate the sample size by considering the following assumptions: 95 % two-sided confidence level, with a power of 80 %. and α error of 5 %. The final maximum sample size taken from output was 98. Thus, the sample size was increased to 100 patients to assume any drop out cases during follow-up[6]

$$\left(\frac{Z_{a/2}+Z_B}{P_1-P_2}\right)^2 (p_1q_1+p_2q_2)$$

(Emine *et al*.[6])

n = sample size.

Z a/2 (The critical value that divides the central 95 % of the Z distribution)

ZB (The critical value that divides the central 20 % of the Z distribution)

p1 = Accuracy prevalence in TCD group

p2 = Accuracy prevalence in FL group.

Ethical consideration and written informed consent: An approval of the study was obtained from Al-Azhar University Academic and Ethical Committee. Every woman signed an informed written consent for acceptance of the process.

Table 1. Age and body mass index (BMI) descriptive study (n = 100).

	Minimum–maximum	Mean ± SD.	Median (interquartile range)
Age (y)	17.0–34.0	26.83 ± 3.22	26.0 (25.0–29.0)
BMI[#] (kg/m^2)	25.0–30.0	27.30 ± 1.53	27.0 (26.0–28.0)

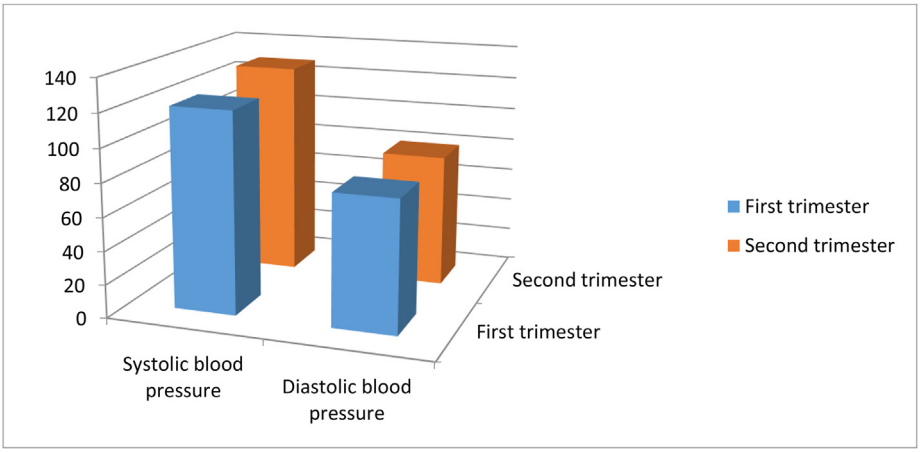

Fig. 1. Comparison between first trimester and second trimester according to blood pressure.

Table 2. Protein in urine mg/day during the first and second trimester of pregnancy (n = 100).

Urine protein (mg/day)	First trimester No. (%)	Second trimester No. (%)	Marginal Homogeneity[a]	*P*
Nil	100 (100.0)	65 (65.0)		
1	0	13 (13.0)		
2	0	21 (21.0)	29.0*	<0.001*
3	0	1 (1.0)		

P: *P* value for comparing between first trimester and second trimester.
[a] MH: Marginal Homogeneity Test.

Statistical analysis of the data: IBM's statistical program, SPSS 20.0, was used to process and analyze the data. IBM Corp., Armonk, New York. Quantitative and percentage descriptions were employed for qualitative information. To ensure a normally distributed sample, we employed the Kolmogorov-Smirnov test. The minimum and maximum values, as well as the mean, standard deviation, median and interquartile range (IQR), were used to characterize the quantitative data. The acquired findings were deemed significant at the 5 % level.

3. Results

Table 1.

The ages of the women in this research are from 17 to 34, as shown in the previous table. The average BMI was 30 (kg/m^2), with a lower limit of 25 (kg/m^2). Included cases had a mean age of 26.83 and a mean body mass index of 27.3 Fig. 1, Table 2.

As regard urine protein, all cases were normal in the first trimester but in the second trimester 20 % of cases had plus 2 proteins in urine and 12 % had plus 1 protein in urine. Urinary protein levels varied significantly among the first and second trimesters Table 3.

This table shows doppler US findings: mean uterine doppler PI, RI was 1.83, 0.78, respectively. Mean β-hCG level was 60743.6 Fig. 2, Table 4.

This table shows the relation between development of PE and the number of fetuses. There was insignificant relation between the number of fetus and cases who developed PE Table 5.

PE is statistically associated with greater PI, RI in the uterine arteries during the first trimester, as seen in the table Fig. 3, Table 6.

Table 3. Descriptive analysis of the studied cases regarding doppler US and beta human chorionic gonadotropin level (n = 100).

Doppler US	Minimum–maximum	Mean ± SD.	Median (interquartile range)
Uterine artery PI	1.50–2.60	1.83 ± 0.33	1.70 (1.60–1.90)
Uterine artery RI	0.71–0.89	0.78 ± 0.05	0.79 (0.73–0.79)
β-hCG level	4567–76899	60743.6 ± 130107	61438 (56732–67892)

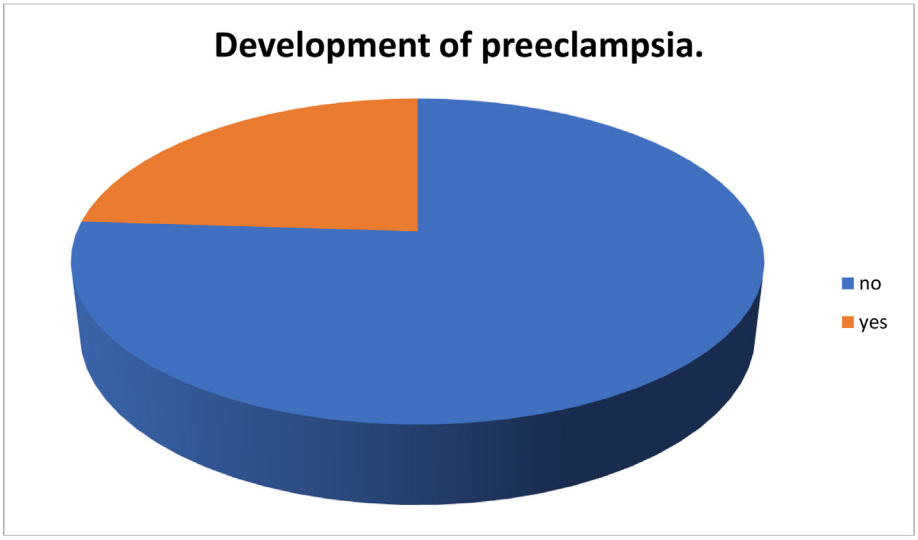

Fig. 2. Preeclampsia incidence and severity among the sample population (n = 100).

Table 4. Relation between cases who developed preeclampsia with the number of fetus (n = 100).

	Cases developed preeclampsia		χ^{2a}	$^{FE}P^{b}$
	No (n = 76) No. (%)	Yes (n = 24) No. (%)		
Number of fetus				
Single	73 (96.1)	23 (95.8)	0.002	1.000
Twins	3 (3.9)	1 (4.2)		

[a] χ^2: Chi square test.
[b] FE: Fisher Exact.

As regard β-hCG level there was a statistically significant relation among lower levels of β-hCG and development of PE Table 7.

This table shows that: at a cut off greater than 1.9, Uterine artery PI had sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were hundred %. At a cut off greater than 0.79, Uterine artery RI had sensitivity, specificity, PPV, NPV were 100 %. At a cut off less than or equal to 45 678, β-hCG level had sensitivity, specificity, PPV, NPV were hundred%.

Table 5. Preeclampsia risk in the first trimester as measured by Doppler ultrasound of the uterine artery (n = 100).

	Cases who developed preeclampsia		t[a]	P
	No (n = 76)	Yes (n = 24)		
Uterine artery PI				
Minimum–maximum	1.50–1.90	2.10–2.60		
Mean ± SD	1.67 ± 0.13	2.34 ± 0.22	14.011*	<0.001*
Median	1.70	2.40		
Uterine artery RI				
Minimum–maximum	0.71–0.79	0.82–0.89		
Mean ± SD	0.76 ± 0.03	0.86 ± 0.03	13.849*	<0.001*
Median	0.75	0.87		

[a] t: Student t-test.

4. Discussion

It is well recognized that PE is a syndrome characterized by chronic hypertension throughout pregnancy. As many as 3 % of first-time mothers and 1–3% of repeat mothers are affected. About 15 % of maternal death in industrialized countries can be attributed to this issue, therefore resulting in maternal and infant mortality and morbidity.[6]

Doppler sonography is able to determine the capability and quality of blood flow, in the minor branches of uterine arteries, and hence the uteroplacental circulation. As a pregnancy progresses, the uterine arteries become less restrictive, allowing more blood to flow through them. Inadequate trophoblastic invasion, on the other hand, causes the uterine arteries to have higher resistance to blood flow.[7]

The main results of this study were as following:

Mean age among included cases was 26.83 years with mean BMI 27.3. As regard number of fetus 96 % of cases had single fetus and twins founded in 4 %. 24 % of cases developed preeclampsia and 76 % had no preeclampsia. There was significant relation between higher age and BMI with occurrence of preeclampsia among included cases.

According to Mohammed *et al.* A total of 436 pregnant females who met the study's criteria & provided written informed consent participated.

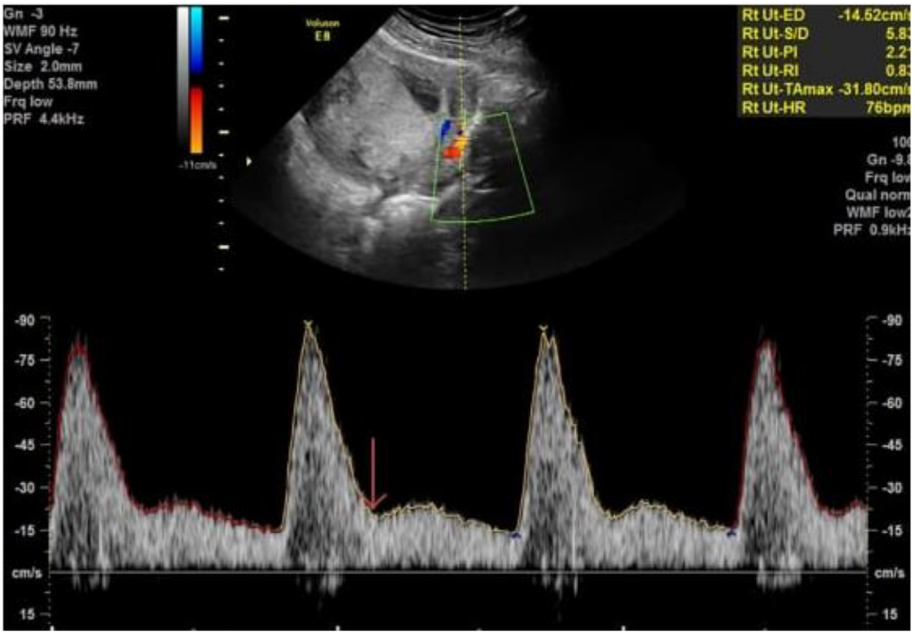

Fig. 3. Transabdominal Doppler interrogation of the uterine artery at the level of the internal cervical os.

Table 6. Relation between cases who developed preeclampsia with beta human chorionic gonadotropin level in the first trimester (n = 100).

	Cases who developed preeclampsia		t[a]	*P*
	No ($n = 76$)	Yes ($n = 24$)		
β-hCG level				
Minimum–maximum	56732.0–76899.0	4567.0–45678.0		
Mean ± SD	66455.71 ± 8061.41	42655.29 ± 8211.14	12.433*	<0.001*
Median	67890.0	43567.0		

[a] t: Student *t*-test.

Only 388 women met the inclusion criteria for the study since 29 were lost to follow-up and 19 had miscarriages. All patients had a sonogram, Doppler of the uterine artery, and serum - β-HCG tested among 11 and 13 + 6 weeks of pregnancy. During the diagnostic follow-up, 58 women had PE, while 330 women had normal blood pressure. Preeclamptic patients were not significantly younger than those who did not develop hypertension during pregnancy. Patients with PE, on the other hand, had a considerably higher mean BMI ($P < 0.001$).[8]

The current research found that in comparison between first and second trimester there was significant increase in systolic blood pressure in second trimester versus first trimester but as regard diastolic blood pressure there was insignificant differences.

In the study of Ismail *et al*. Seventy-five percent of pregnant women who experience a diastolic notch in their first trimester will go on to have PE.[9]

The mean arterial blood pressure of preeclamptic women was found to be greater than that of

Table 7. Validity (AUC, sensitivity, specificity) for doppler ultrasound and beta human chorionic gonadotropin levels for detection of preeclampsia.

	AUC	*P*	95 % C.I	Cut off[b]	Sensitivity	Specificity	PPV	NPV
Uterine artery PI	1.000	<0.001[a]	1.0–1.0	>1.9	100.0	100.0	100.0	100.0
Uterine artery RI	1.000	<0.001[a]	1.0–1.0	>0.79	100.0	100.0	100.0	100.0
β-hCG level	1.000	<0.001[a]	1.0–1.0	≤45 678	100.0	100.0	100.0	100.0

AUC, Area Under a Curve; CI, Confidence Intervals; NPV, Negative predictive value; PPV, Positive predictive value.
[a] Statistically significant at *P* less than or equal to 0.05.
[b] Cut off was choosed according to Youden index.

nonpreeclamptic women at the end of the first trimester (90.8 ± 9.7 vs. 83.1 ± 8.4 mm Hg, $P < 0.001$).[10]

The current study showed that as regard urine protein, all cases was normal in first trimester but in second trimester 20 % of cases had plus 2 proteins in urine and 12 % had plus 1 protein in urine.

In the study of Kashinakunti *et al*. 52 patients with PE took part in the research. Urinary protein levels ranged from 1643.3 ± 2079.5 mg/day on average.[11]

In the study in our hands, as regard doppler US findings, mean uterine doppler PI, RI was 1.83, 0.78, respectively. There was significant relation among higher uterine artery PI, RI and cases developed PE. Using ROC curve, at a cut off greater than 1.9, The sensitivity, specificity, PPVand NPV of the PI for the uterine artery were all perfect. Uterine artery RI had 100 % sensitivity, specificity, PPV, and NPV at a cut off of greater than 0.79.

Similar results were found by Mittal *et al*., who found that PE was linked to higher mean PI and RI in the uterine artery during the first trimester, but that the mean RI was a more accurate predictor than the mean PI. Based on the results of the ROC analysis, the optimal PI cutoff value for RUAs is 1.5, the optimal PI cutoff value for LUAs is 1.4, and the optimal RI cutoff value for both is 0.65.[12]

Our results showed that the mean β-hCG level was 60743.6. As regard β-hCG level there was significant relation between lower levels of β-hCG and development of PE. Using ROC curve, at a cut off less than or equal to 45 678, β-hCG level had sensitivity, specificity, PPV, NPV were 100 %.

Our findings were consistent with those of Johnson *et al*., who examined 62 pregnancies created with IVF/ET and assessed maternal serum HCG levels at 7–13 weeks of gestation. The eight women who ended up with PE had significantly lower levels of β-HCG.[13]

Our finding was supported by the research of Abdel Moety *et al*., who showed that serum β-hCG was significantly lower in individuals who had PE matched to those who did not.[14]

As for the apparent difference in serum concentrations of HCG during the first and second trimester, Ong *et al*. hypothesized that it was due to impaired placentation and a smaller placental mass in pregnancies progressing to late PE.[15] However, increased levels may be explained by hypoperfusion-related activation of production of this hormone during the second trimester.[16]

While we found a statistically significant difference between preeclamptic and nonpreeclamptic women in terms of maternal serum β-HCG levels, Ismail *et al*.[9]

4.1. Conclusion

PE was linked to low levels of -hCG in the first trimester and elevated PI and RI in the mother's uterine artery.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflicts of interest

The authors declared that there were NO conflicts of Interest.

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