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ORIGINAL ARTICLE

Role of First Trimesteric Uterine Artery Doppler and Maternal Serum Beta Human Chorionic Gonadotropin (β-HCG) Levels in Prediction of Preeclampsia and Fetal Growth Restriction

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Abstract

Background: **Preeclampsia develops in the placenta, beginning with insufficient cytotrophoblastic invasion and concluding with extensive endothelial dysfunction in the mother. Elevated 1st trimester uterine artery mean resistivity index (RI) is significantly connected with fetal IUGR. Serum β-hCG levels in the 1st trimester can predict pregnancies that subsequently develop preeclampsia and associated fetal IUGR.**

Objective: **To study the role of first trimester maternal uterine artery Doppler and serum Beta human chorionic gonadotropin (β-hCG) in prediction of preeclampsia and intrauterine growth restriction.**

Patients and methods: **This study analyzed data from pregnant women who went to the obstetric out-patient clinic at Al-Azhar University in Cairo, Egypt, as part of their regular prenatal treatment at 11−14 weeks of gestation they were subdivided into a case group (A) and a control group (B). The case group consists of 80 females.**

Results: **A statistically significant distinction existed among the 2 groups regarding to BHCG level, Mean RT uterine artery RI&PI, Mean LT uterine artery RI&PI, Presence of diastolic notch in uterine artery, Gestational age and Development of preeclampsia. There was no statistically significant variance among the 2 groups regarding to Maternal age.**

Conclusion: **Abnormal uterine artery Doppler studies in the first and second trimesters have been linked to adverse pregnancy outcomes such as preeclampsia, fetal growth restriction and perinatal mortality. On the other hand, Doppler testing appears to have a limited predictive value in women at low risk, and there are no measures available to avoid unfavorable outcomes based on aberrant results.**

Keywords: Doppler, IUGR-BHCG, Preeclampsia

1. Introduction

Preeclampsia is a pregnancy-related systemic disorder determined by the onset of proteinuria and hypertension. Preeclampsia is linked to considerable maternal and fetal morbidity and death.[1]

Beginning with insufficient cytotrophoblastic invasion and concluding with extensive endothelial dysfunction, preeclampsia develops in the placenta.[1]

Placental anti-angiogenic factors, including soluble FMS-related tyrosine kinase 1 and soluble endoglobin, are elevated in synthesis during preeclampsia.[2]

These placental anti-angiogenic substances are released into the maternal circulation; their effects perturb the maternal endothelium, resulting in hypertension, proteinuria and further preeclamptic systemic symptoms. This infections' molecular mechanism for placental dysregulation is unknown.[2]

Doppler ultrasonography is a non-invasive method for researching the utero-placental circulation; it allows for a qualitative assessment of blood flow in minor branches to the uterine arteries; and,

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in a healthy pregnancy, the impedance to flow in the uterine arteries reduces as the baby grows.[3]

Nevertheless, Doppler investigations demonstrated greater impedance to flow in the uterine arteries in situations of impaired trophoblastic invasion, since these arteries failed to mature into low resistance vessels. Doppler screening investigations done among 11 and 14 weeks of gestation can indicate a correlation among elevated flow impedance in the uterine arteries and the eventual development of hypertensive diseases and its consequences connected to pregnancy.[4]

Moreover, multiple studies shown that an increased mean resistivity index (RI) in the uterine artery during the 1st trimester is substantially related to fetal IUGR.[3]

β-hCG is predominantly produced by the placenta. This encouraged several clinical studies to demonstrate that early placental vascular damage leading to reduced O_2 supply might result in increased maternal serum β-hCG by hyperplasic trophoblastic cells.[5]

Serum beta-hCG levels in the first trimester have been shown by several authors to be a predictor of preeclampsia and fetal IUGR.[3]

2. Patients and methods

At Al-Azhar University hospitals in Cairo, Egypt, During 11–14 weeks of gestation, pregnant women who visited the obstetric out-patient clinic for standard prenatal care examination were separated into a case group (A) and a control group (B). The case group consists of females at high risk for development of pregnancy-related hypertensive diseases like (previous pregnancies complicated by hypertensive disease; maternal history of chronic renal disease; maternal autoimmune disease) and their complications. The control group consists of females free of that risk.

2.1. The inclusion criteria were

Females with single pregnancy, Females with regular menstrual cycles before pregnancy, Females with known date of last menstrual period and Females with gestational age ranging from eleven to fourteen weeks estimated from the 1st day of the last normal menstrual period.

2.2. The exclusion criteria were

Females with diabetes mellitus (DM), Females with multiple pregnancies, Females with pyelonephritis and Females with thyrotoxicosis.

2.3. Methods

Patients were examined after giving their verbal agreement, and their medical histories were thoroughly analyzed (including their reproductive, obstetric, birth control, and menstrual histories, as well as their personal and family histories). All pregnant women were undergo *trans*-abdominal uterine artery Doppler assessment. The transducer will be implanted longitudinally in the right or left lower quadrant of the abdomen to capture recordings from the right or left uterine artery (iliac fossa just above the inguinal ligament). Serial measurements of symphysis fundal height, along with other parameters such as abdominal circumference, estimated fetal weight, amniotic fluid volume, and doppler assessment of the uterine, umbilical, middle cerebral artery, and ductus venosus, were taken from all participants and plotted on a specialized chart to diagnose fetal growth restriction.

2.4. Data management

Numerical variables will be provided as mean ± SD, while categorical variables will be presented as number of instances and percentage, all within the context of an SPSS analysis.

The Student t-test will be used to compare quantitative variables amongst groups. For doing group comparisons on categorical variables, we will utilize the χ^2 test or the fisher exact test, as applicable.

3. Results

Table 1.

The average age of case group was 31.6 years and in the control group was 32.7 years. The variance was statistically insignificant ($P = 0.23$) (Table 2).

With regards to the mean value of beta-hCG, there was a significant statistical distinction among the case and control groups (P value: 0.001) (Fig. 1, Table 3).

When comparing both groups, the control group had considerably lower mean RI & PI of the right uterine artery ($P = 0.0001$ for PI and 0.001 for RI) (Fig. 2, Table 4).

Table 1. Maternal age (years) in the case group and control group.

	Case group ($n = 80$)	Control group ($n = 80$)
Range	18–43	23–43
Mean ± SD	31.6 ± 6.05	32.7 ± 5.56
P value	0.233 (NS)	

Table 2. BHCG level in case and control group.

	Case group (n = 80)	Control group (n = 80)
Range	33,210–82000	38,700–151,971
Mean	43626.33	75551.11
SD	11484.40	25347.54
P value	0.001 (S)	

In the control group, both the mean RI & PI of the left uterine artery were considerably lower than in the case group (Table 5).

The proportion of patients in the case group with positive diastolic notching was substantially higher than those in the control group (P value = 0.002) (Figs. 3 and 4, Table 6).

Comparing the average gestational age at delivery in the case and control groups. There was a statistically significant distinction among the case group's 34.5 weeks and the control group's 39 weeks (P value = 0.043) (Table 7).

Comparison between case group and control group regarding development of preeclampsia. It was cases in a case group (57.5%) and 8 cases in control group (10%) and There was a substantial statistical distinction (P value = 0.001).

4. Discussion

Conversion of spiral arteries to the uteroplacental artery is an essential step in the development of the placental blood supply's physiology. Inadequate trophoblastic infiltration of the placental vascular bed has been linked to a number of poor pregnancy outcomes, including IGR and preeclampsia.[6]

Patients in our research varied in age from 18 to 43, with an average age of 31.6. This contradicted the findings of a research conducted by Pongro jpaw and colleagues in 2010 in which the average age of participants was 36.8 years. The patients in our study tended to be younger, which may be due to the cultural norm of having children at a young age.

The majority of our patients who did not develop preeclampsia gave birth among 37 and 41 weeks of pregnancy (mean value: 39 weeks), while the gestational ages of our patients who did develop preeclampsia ranged from 33 to 36 weeks (mean value: 34 weeks).

This goes with the work of **YU and colleagues.**[7] They showed that whereas the average gestational age at birth for healthy individuals was 40 weeks, it was only 37 weeks for those who had acquired preeclampsia. This difference might be due to that most of our patients who developed preeclampsia had severe degree and had to be terminated prematurely.

Our study can be criticized for its small sample size, as 46 out of 80 patients (57.5%) developed preeclampsia in the case group and about 8 of 80 patients (10%) developed preeclampsia in control group, while in the work of **Pongrojpaw and**

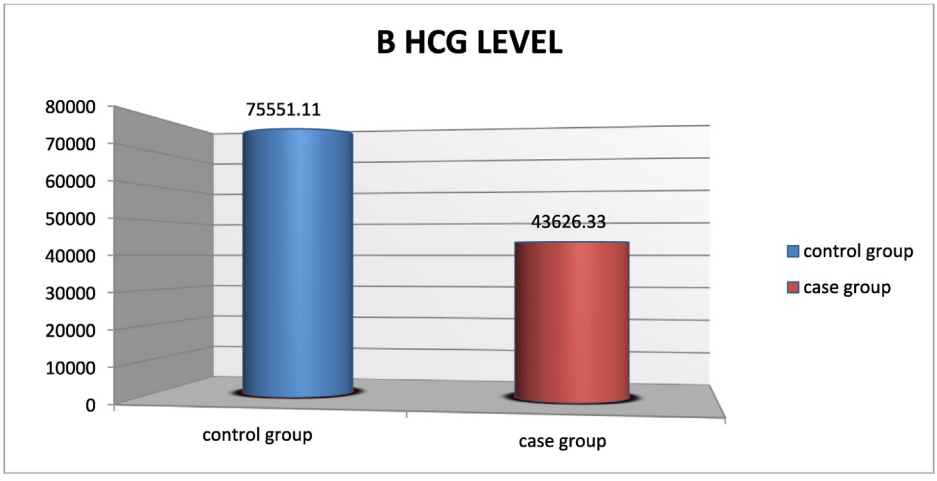

Fig. 1. BHCG level in case and control group.

Table 3. Comparing case with control group means for RT uterine artery RI&PI.

	Case group		Control group	
	RI	PI	RI	PI
Mean ± SD	0.86 ± 0.11	2.15 ± 0.48	0.71 ± 0.12	1.54 ± 0.44
P value	0.001 for PI and 0.001 for RI			

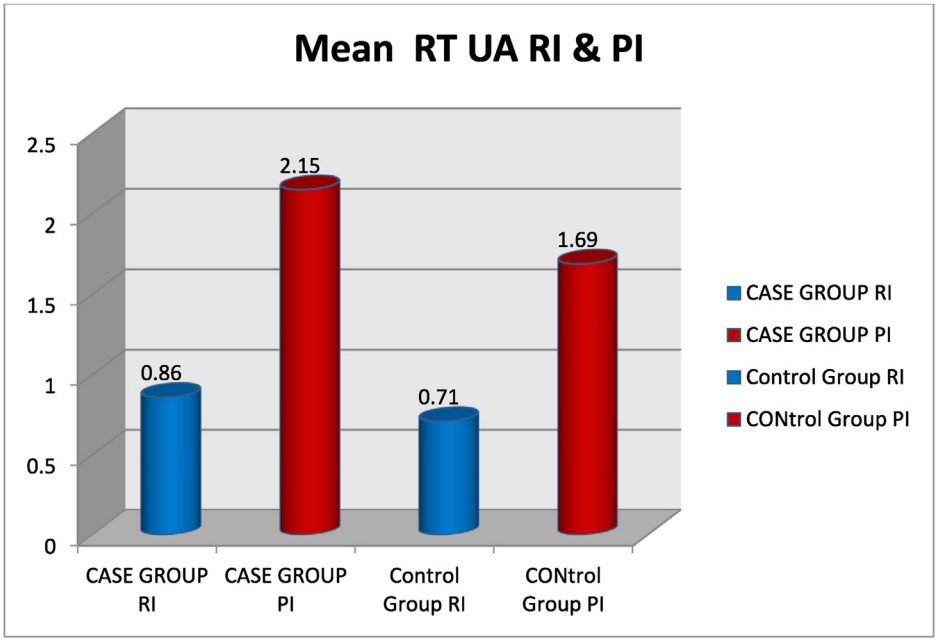

Fig. 2. Mean RT uterine artery RI&PI in case and control group.

Table 4. Mean LT uterine artery RI&PI in case and control group.

	Case group		Control group	
	RI	PI	RI	PI
Mean ± SD	0.957 ± 0.47	2.07 ± 0.54	0.707 ± 0.11	1.507 ± 0.38
P value	0.001 for PI and 0.001 for RI			

Table 5. Presence of diastolic notch in uterine artery in case and control group.

	Case group	Control group
Absent		
Count	34	72
Percent	42.5%	90%
Present		
Count	46	8
Percent	57.5%	10%
P value	0.002	

colleagues,[8] 27 out of 330 patients developed preeclampsia (8.18%). The higher percentage of those who developed preeclampsia in case group in our study can be explained by that we studied high risk patients (e.g. with chronic hypertension, renal diseases, intrauterine growth restriction (IUGR) and intrauterine fetal death (IUFD), previous history of preeclampsia or smokers) while they studied low risk population and also due to their larger sample size.

In our study, 35 cases had associated IUGR with severe preeclampsia (43.75%) in the case group and delivered at gestational periods of 33 and 34 weeks respectively. Pongrojpaw and colleagues in 2010 stated that 16 patients had associated IUGR with Preeclampsia (4.84%).

Increased mid-pregnancy uterine artery impedance is linked to a higher risk of preeclampsia and/or SGA.[9]

In our study, 54 cases showed changes with uterine artery Doppler in the form of PI > 1.45, RI > 0.58, Unilateral or Bilateral notching in which 46 cases developed preeclampsia.

Among the case group, there was a statistically significant correlation amongst the changes of uterine artery Doppler and the development of preeclampsia (*P* value < 0.05) as well there was statistically significant correlation among the same changes and gestational period at delivery (*P* value < 0.05).

This was consistent with the work of **Yu and colleagues**.[7] who detected similar results with statistically significant association (*P* value < 0.0001).

In his study, an early diastolic notch appeared before 28 weeks of gestation and was connected to adverse pregnancy outcomes, moreover he categorized the notch according to its depth using notch index and observed adverse pregnancy outcomes with the group having deeper notch & hence

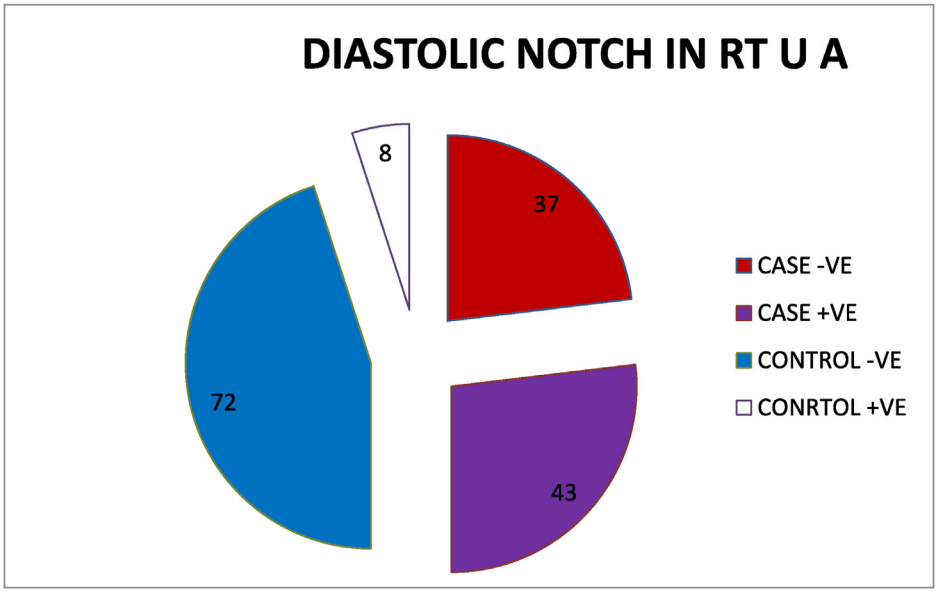

Fig. 3. Diastolic notch in RT UA in case and control group.

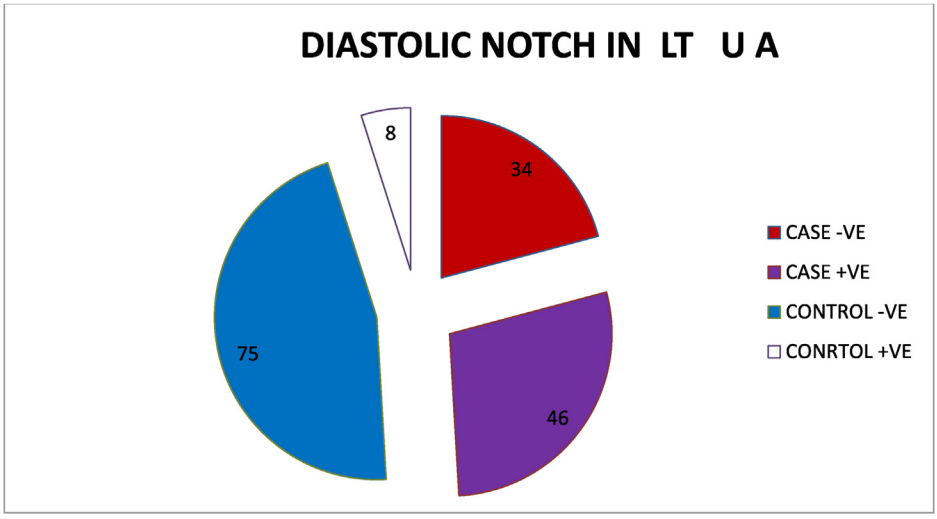

Fig. 4. Diastolic notch in LT U A in case and control group.

Table 6. Gestational age in case and control group.

	Case group	Control group
Range	33–36	37–41
Mean ± SD	34.5 ± 0.5	39 ± 0.5
P value	0.043 (S)	

Table 7. Development of preeclampsia in case and control group.

	Case group	Control group
Absent		
Count	34	72
Percent	42,5%	90%
Present		
Count	46	8
Percent	57.5%	10%
P value	0.01	

concluded that it is not the presence of early diastolic notch merely, but its depth is the most important predictor regarding poor pregnancy consequences.

The mean value of maternal serum β-hCG was observed to be considerably lower in females who had pre-eclampsia and IUGR (case group) compared to females who did not develop either of these conditions (control group) with a significant statistical distinction ($P < 0.001$).

These results are in accordance with **Johnson and colleagues.**[10] analyzed the levels of -human

chorionic gonadotropin in the mothers' blood between 7 and 13 weeks of pregnancy in 62 pregnancies resulting from in vitro fertilization and embryo transfer. Among the eight women who later had preeclampsia, they discovered considerably lower levels of β-hCG.[10]

Also, **Pedersen and colleagues**[11] analyzed the concentrations of maternal serum β-hCG between weeks eight and fourteen in 93 pregnancies and found that the prevalence of preeclampsia was considerably higher in pregnancies with lower β-hCG concentrations.[11]

4.1. Conclusion

Preeclampsia, fetal growth limitation, and neonatal death have all been linked to abnormal uterine artery Doppler investigations in the 1st and 2nd trimesters. Nevertheless, there appears to be a limited predictive value of Doppler testing in a low-risk population of females, and there are presently no therapies available to avoid ill outcomes based on aberrant results. Women who have an abnormal uterine artery Doppler study performed early in pregnancy who are otherwise thought to be at low risk require access to effective therapies to prevent adverse late pregnancy outcomes.

Authorship

All authors have a substantial contribution to the article.

Disclosure

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

Conflicts of interest

The authors declared that there were no conflicts of interest.

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