Uterine Doppler Abnormalities as Prognostic Indicators for Preeclampsia in High-Risk Pregnancies

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ABSTRACT

Background: Preeclampsia is associated with significant maternal and neonatal morbidity and mortality. Doppler ultrasound makes it possible to determine the flow of a blood vessel quantitatively or qualitatively. **Objective**: to measure the association between abnormal uterine artery Doppler flow rate during the second trimester of pregnancy and the occurrence of preeclampsia in Iraqi women with high-risk pregnancy. **Patients and method**: A prospective cohort study was conducted between March 1, 2023 and February 28, 2024 in patients treated in our unit in the hospital with some comorbidity and with 20 to 24 weeks of pregnancy. patients with a diagnosis of high-risk pregnancy due to maternal comorbidities, between 20 and 24 weeks of gestation, with a single live fetus and who agreed to join the study were included. **Results**: Eight-two patients were examined and categorized into two groups. The incidence of preeclampsia was significantly greater in the cohort exhibiting aberrant uterine Doppler flow (36% vs to 12.2%; p < 0.001; relative risk [RR] 4.1; 95% confidence interval [CI]: 1.3-12.87). Maternal problems were more prevalent, with a higher rate of intensive care admissions for preeclampsia (22% versus 2.4%; p < 0.001; OR 1.3; 95% CI: 1.3-93.5). Perinatal outcomes indicated an elevated risk of low birth weight (p < 10%; OR 3.5; 95% CI: 1.4-9.1 and p < 3%; OR 3.3; 95% CI: 3.3-9.8) and neonatal intensive care unit admission (OR 1.2; 95% CI: 1.1-1.5). **Conclusion**: Abnormal uterine Doppler flow in the second trimester is significantly associated with preeclampsia, severe maternal complications (admission to intensive care) and adverse neonatal outcomes (low weight, admission to intensive care) in high obstetric risk pregnancies

Keywords: High-Risk Pregnancies, Preeclampsia, Uterine Doppler, Abnormalities

1. INTRODUCTION

Any medical condition that is associated with a real or potential danger to the health or well-being of the mother or the fetus is considered a high-risk pregnancy [1]. The prevalence of this is about 15-20% [2]. Hypertensive disorders of pregnancy constitute one of the main causes of maternal and perinatal mortality worldwide [3]. Preeclampsia is associated with significant maternal and neonatal morbidity and mortality. Several studies have shown that increased vascular resistance is an indicator of placental insufficiency [4-6]. The speed of the circulating blood depends on the distal vascular resistance of the distribution network, the force that the heart impresses when contracting and the viscosity of the blood [7]. Doppler ultrasound makes it possible to determine the flow of a blood vessel quantitatively or qualitatively. There are three impedance indices that provide information about vascular resistance, which is considered the main determinant of blood flow: 1] the pulsatile index, 2] the resistance index and 3] the systole-diastole ratio index [8,9]. The most prominent components of Doppler flowmetry are the systolic and diastolic velocity. The difference between one and the other is pulsation. The pulsatile index allows determining whether there is a high or low resistance of the vessel to the passage of blood flow, so it is considered a quantitative parameter of vascular resistance. It is normal that the average pulsatile index of the uterine arteries decreases throughout pregnancy as a result of the progressive decrease in the resistance of the uteroplacental circulation as more weeks of gestation pass [10-12]. For the measurement of the pulsatile index of the uterine arteries, a sagittal section of the uterus is obtained and the duct and the internal cervical orifice are identified. Then, with the transducer at the midline, it is gently tilted to one side and a color flow mapping is used to identify each uterine artery along the side of the cervix and the uterus at the height of the internal orifice. Pulsed wave Doppler is used with the sampling gate set at 2 mm to cover the entire vessel, with due care to ensure that the sound angle is less than 30°. When three similar consecutive waveforms are obtained, the pulsatile index is measured and the average of the left and right uterine arteries is calculated [13,14]. The average pulsatile index of the uterine arteries has a normal distribution according to the weeks of pregnancy and is considered abnormal when it is greater than the 95th percentile [15]. The Doppler flowmetry of the abnormal uterine arteries. A. It corresponds

to the Doppler flowmetry of the right uterine artery in a woman with the pulsatile index lower than the 95th percentile at 24 weeks of gestation, the blood flow is greater. B. it corresponds to the Doppler flowmetry of the uterine artery with an abnormal pulsatile index [greater than the 95th percentile] of a woman diagnosed with gestational hypertension and fetal growth restriction at 24 weeks. A decrease in uterine flow and the presence of the protodiastolic notch or "notch" can be observed. it is associated with complications: intrauterine growth restriction, preeclampsia and fetal death before the most obvious clinical signs of these conditions manifest themselves [16]. The aim of this study was: to measure the association between abnormal uterine artery Doppler flow rate during the second trimester of pregnancy and the occurrence of preeclampsia in Iraqi women with high-risk pregnancy.

2. METHODOLOGY

A prospective cohort study was conducted between March 1, 2023 and February 28, 2024 in patients treated in our unit in the hospital with some comorbidity and with 20 to 24 weeks of pregnancy.

Inclusion criteria: patients with a diagnosis of high-risk pregnancy due to maternal comorbidities, between 20 and 24 weeks of gestation, with a single live fetus and who agreed to join the study.

Exclusion criteria: patients with a diagnosis of a fetus with major malformations or with abnormal insertion of the placenta.

Elimination criterion: patients who did not continue prenatal control in the participating unit. The type of sampling was non-probabilistic of consecutive cases. The measurement of the average pulsatile index of the uterine arteries was carried out with a Voluson MR GE brand Doppler ultrasound.

The group of exposed patients was integrated with those who had abnormal uterine artery Doppler flow measurement [more or less greater than the 95th percentile for weeks of pregnancy] and the group of unexposed by patients who had a normal uterine artery pulsatile index [less than the 95th percentile for weeks of gestation] according to the reference tables of Gómez O et al. [12]

The follow-up of the patients was continued until the termination of pregnancy. The proportion of patients with preeclampsia was compared between one group and the other.

This was diagnosed according to the criteria of the American College of Obstetrics and Gynecology [17].

Statistical analysis

The sample size was calculated with the statistical program Epi Info™ version 7.2 for a cohort study with the following parameters: a two-tailed confidence level of 95%, a statistical power of 80%; an exposed-unexposed ratio equal to 1; an expected outcome in the unexposed group of 6% (preeclampsia); and an expected outcome in the exposed group of at least 30%. The resulting sample size was 82 patients (41 in the exposed group and 41 in the unexposed group) using the Kelsey formula. A descriptive analysis was carried out in each group studied, with summary and dispersion measures appropriate for each variable. With the Student's t-test for unrelated samples, it was determined whether there was a difference in the means of the continuous random variables between the two groups or with the Mann-Whitney U-test according to the type of distribution of the data. X2 was used for the comparison of the different proportions between the groups. By calculating the ratio of mummies and the 95% confidence intervals, the strength of association between the variables of interest was determined. When the p-value was less than 0.05 at two tails, it was considered statistically significant. The database was analyzed in the statistical program IBM-SPSS version 27.

All patients voluntarily agreed to collaborate by means of an informed consent. There is no conflict of interest on the part of any of the members of the research group.

3. RESULTS

A total of 82 patients with high-risk pregnancies were included, of them 41 had abnormal uterine artery Doppler flowmetry (exposed group). The clinical and demographic characteristics of the patients included in the study are shown in (**Table 1**). Blood pressure was higher in patients with abnormal Doppler flow of the uterine arteries. Patients with normal Doppler flow measurement of the uterine arteries had a higher frequency of hypothyroidism. There were no significant differences in age, body mass index, parity, obesity, gestational diabetes, type 2 diabetes mellitus, hypothyroxinemia, antiphospholipid antibody syndrome and rheumatoid arthritis between one group and the other.

The reports of the Doppler ultrasound performed during the second trimester of pregnancy were shown in (**Table 2**). There were no differences in the average fetometry or in the estimated fetal weight between the two groups. The pulsatile index of the right and left uterine artery and the mean pulsatile index of the uterine arteries were higher in the exposed group (1.22 compared to 0.65; p > 0.001). Maternal complications are reported in (**Table 3**). There was no significant difference in the route of termination of pregnancy, the majority was by cesarean section. A higher frequency of hypertensive disease, gestational hypertension, preeclampsia without severity criteria, preeclampsia with severity criteria and HELLP syndrome was observed in the patients of the exposed group (p < 0.05). There were no cases of eclampsia in any of the groups. The perinatal outcomes of the patients' children are reported in Table 4. Patients with abnormal Doppler flowmetry of the uterine arteries had a child with lower weight, smaller height, with fewer weeks of gestation. There was a higher proportion of newborns weighing less than the 10th percentile and weighing less than the 3rd percentile (p < 0.05). There was also a higher proportion of admissions to the pathological nursery and to the neonatal intensive care unit. Two perinatal deaths were recorded in the exposed group. There were no significant differences in the Apgar at one minute and at five minutes between one and the other group. Association between Doppler flowmeter of the uterine arteries and maternal and perinatal complications. The association between abnormal Doppler flowmeter of the uterine arteries and the risk of adverse events is shown in Table 5. Patients in the exposed group had an increased risk of suffering from preeclampsia 4.5 (95% CI: 1.7-11.9), admission to the adult intensive care unit 11.2 (95% CI: 1.3-93.5), low birth weight newborn (greater than the 10th percentile and greater than the 3rd percentile) and an increased risk of their child being admitted to the intensive care unit 1.2 (95% CI: 1.1-1.5)

Table 1. Clinical and demographic characteristics

Variable	Study group (n=41)	Control group (n=41)	P. value
Age (years); mean (SD)	31.8 (5.6)	29.9 (6.4)	0.162
Body mass index (kg/m²); mean (SD)	33.24 (7.3)	30.9 (4.6)	0.870
Systolic blood pressure (mmHg); mean (SD)	137 (18.4)	124.9 (17)	0.002*
Diastolic blood pressure (mmHg); mean (SD)	86.37 (17.8)	76.2 (14.8)	0.002*
Primigravida; n (%)	15 (36.6)	12 (29.3)	0.481
Pregnancy; medium (range)	2 (1-5)	2 (1-6)	0.499
Obesity; n (%)	27 (65.9)	23 (56.1)	0.360
Gestational diabetes; n (%)	16 (39.0)	17 (41.5)	0.822
Type 2 diabetes mellitus; n (%)	3 (7.3)	2 (4.9)	0.640
Hypothyroidism; n (%)	16 (39.0)	27 (65.9)	0.015*
Hypothyroxinemia; n (%)	4 (9.8)	7 (17.1)	0.331
APS; n (%)	3 (7.3)	2 (4.9)	0.640
Rheumatoid arthritis; n (%)	1 (2.4)	0 (0.0)	0.314

Study group: patients with Abnormal DFUtA; PI ≥ 95th percentile for the weeks of pregnancy
Control group: patients with normal DFUtA; PI < 95th percentile for the weeks of pregnancy
ASP: Antiphospholipid syndrome
*Significant, SD: standard deviation, APS: PI: Pulsatility index

Table 2. Ultrasound results of the second trimester of pregnancy

Variable	Study group (n=41)		Control group (n=41)		P. value
	Mean	SD	Mean	SD	
Mean fetometry (weeks)	22.9	2.70	21.30	1.70	0.619
Estimated fetal weight (gram)	576.0	222.9	614.7	180.8	0.769
PI Right uterine artery	1.12	0.68	0.64	0.29	<0.001*
PI Left uterine artery	1.31	0.82	0.66	0.32	<0.001*
Mean PI of Uterine arteries	1.22	0.57	0.65	0.18	<0.001*

* Significant, SD: standard deviation

Table 3. Maternal complications

Variable	Study group (n=41)		Control group (n=41)		P. value
	No.	%	No.	%	
Cesarean section	31.0	75.61	29.00	70.73	0.618
Admission to ICU	9.0	21.95	1.00	2.44	<0.001*
PIH	23.00	56.10	9.00	21.95	<0.001*
Gestational hypertension	8.00	19.51	4.00	9.76	
PE without severity criteria	2.00	4.88	1.00	2.44	
PE with severity criteria	11.00	26.83	4.00	9.76	0.028*
HELLP syndrome	2.00	4.88	0.00	0.00	
Eclampsia	0.00	0.00	0.00	0.00	

* Significant, PIH: pregnancy induced hypertension, PE: preeclampsia

Table 4. Perinatal outcomes

Variable	Study group (n=41)	Control group (n=41)	P. value
Weight of newborn (gram), mean (SD)	2341 (855)	2710 (562)	0.023*
Height (cm), mean (SD)	44 (6)	50 (6)	0.013*
Apgar score at 1 minute; median (range)	8 (2-9)	8 (5-9)	0.762
Apgar score at 5 minutes; median (range)	9 (5-9)	9 (7-9)	0.870
Gestational age (weeks), mean (SD)	35.9 (3.6)	37.2 (2.7)	0.810
Newborn weight < 10th percentile; n (%)	7 (17.1)	4 (9.8)	0.007*
Weight of newborn <3rd percentile; n (%)	15 (36.6)	6 (14.6)	0.023*
Admission to NICU; n (%)	9 (22.0)	0 (0)	0.004*
Perinatal death; n (%)	2 (5.4)	0 (0)	0.474

*Significant, NICU=neonatal intensive care unit

Table 5. Association between abnormal doppler flow measurement of uterine arteries and the risk of preeclampsia

Variable	Study group (n=41)		Control group (n=41)		OR (95% CI)	P. value*
	No.	%	No.	%		
PIH	23	56.1	9	22.0	4.5 (1.7-11.9)	0.003
Preeclampsia	15	36.6	5	12.2	4.1 (1.3-12.9)	0.021
Admission to ICU	9	22.0	1	2.4	11.2 (1.3-93.5)	0.018
Weight of newborn <10%	22	53.7	10	24.4	3.5 (1.4-9.1)	0.013
Weight of newborn <3%	15	36.6	6	14.6	3.3 (1.1-9.8)	0.043
Admission to the NICU	9	22.0	0	0.0	NA	0.001

PIH: pregnancy induced hypertension, ICU: intensive care unit (adult), NICU: neonatal intensive care unit, OR: odds ratio, 95%CI: 95% confidence interval
NA: not applicable due to division by zero
P. value is significant in all comparisons, P<0.05

4. DISCUSSION

The study demonstrates that ultrasound findings of abnormality in the Doppler flowmetry of the uterine arteries during the second trimester in patients with high-risk pregnancies are associated with adverse maternal and perinatal outcomes: preeclampsia, fetal growth restriction and perinatal death. What is reported here seeks to determine its usefulness in this context, where clinical heterogeneity can alter its predictive value. Patients with comorbidities are more likely to suffer from maternal and perinatal adverse events [18]. It is reported that the observed changes in Doppler flowmetry are a consequence of increased vascular resistances which, in turn, are caused by the imbalance between pro- and anti-angiogenic factors. All these changes culminate in systemic endothelial dysfunction, which is part of the pathophysiology of placental insufficiency that causes preeclampsia and fetal growth restriction [19]. In congruence with the results, it is reported that patients with preeclampsia have a higher average pulsatile index of the uterine arteries compared to healthy patients, which allows identifying those who are at greater risk of complications during pregnancy: preeclampsia and fetal growth restriction [20,21]. It is also reported that histopathological placental lesions that result in increased resistance to blood flow may be the cause of fetal death [22]. Likewise, it has been reported that placental vascularization is useful for predicting

preeclampsia and fetal growth restriction at different stages of gestation and that the uterine artery pulsatile index is an early predictor of an adverse outcome in patients with clinical confirmation of placental insufficiency [23]. Similar to what is reported here, there are reports of abnormal Doppler flowmeter findings of the uterine arteries that are associated with a high risk of maternal and neonatal complications in complicated pregnancies with early-onset preeclampsia [24]. Several researches propose to combine the Doppler flow measurement of uterine arteries with biomarkers [25]. The combination of the Doppler flowmetry of the uterine arteries with the ratio sFlt-1/PLGF, soluble endoglin, with the placental brain index or with the platelet index in high-risk pregnancies, the performance of this test increases for the early identification of risk of adverse outcomes that may contribute to implementing some early intervention [26-28]. Doppler flow measurement of the uterine arteries is not an invasive procedure: it is simple, safe and reproducible. It can even be practiced in the bed of high-risk and unstable patients [29]. It can help the obstetrician-gynecologist to accurately assess fetal well-being in high-risk pregnancies in order to improve maternal and perinatal outcomes [30].

Strength of the study

A strength of this study is that all the patients had a high-risk pregnancy and that the ultrasound determinations were made by certified and trained medical specialists. Another is that the abnormalities in the flowmetry were detected by Doppler ultrasound between 21 and 22 weeks, long before the clinical manifestations of the disease began in patients who subsequently resulted in preeclampsia or adverse outcomes.

Limitation of the study

The authors are aware of the limitations of this study, such as the heterogeneity of high-risk diagnoses and the few patients included. Despite this, the sample size was calculated to determine differences in proportions, which was successfully achieved. Another limitation of uterine artery Doppler measurement is intra- and interobserver variability; however, it has been reported that the determination of uterine artery Doppler flowmeter is the most reproducible.

Finally, we can affirm that Doppler ultrasound of the uterine arteries in the second trimester is a useful method for screening patients with high-risk pregnancy. It is non-invasive, low-cost and available in almost all hospitals of the second and third level of care. The correct use of

this tool during the second trimester could help the early identification of patients who, perhaps, could experience adverse events during pregnancy and, with this, there would be an opportunity to reduce maternal and perinatal morbidity and mortality through the implementation of timely interventions.

The pulsatile index is the most widely used in maternal fetal medicine because it is the most reproducible, objective and effective for the screening of patients at high risk of maternal and perinatal complications; in addition, it correlates with the clinical severity of complications, such as preeclampsia.

The results support the use of uterine Doppler as an accessible method in environments with limited resources, where other markers such as sFlt-1/PlGF are not available.

5. CONCLUSIONS

Abnormal uterine Doppler flow in the second trimester is significantly associated with preeclampsia, severe maternal complications (admission to intensive care) and adverse neonatal outcomes (low weight, admission to intensive care) in high obstetric risk pregnancies.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association , 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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