Original Article

Uterine Artery Doppler Disorder and Its Association with Demographic Characteristics of Patients Referring for First Trimester Screening

Mahsa Sadeghi[1], Mahin Najafian[1], Sara Masihi[1], Elham Farhadi[2], Razieh Mohamadjafari[1*]

[1]Fertility, Infertility and Perinatology Research center department of Obstetric and Gynecology Ahvaz Jundishapur University of Medical Science, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[2]Clinical Research Development Unit, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[1*]Adress correspondence to this author at the fertility infertility and perinatology research center Department of Obstetric and Gynecology, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.Email:Rmj417072@gmail.com

najafian-m@ajums.ac.ir1, mohamadjafari-r@ajums.ac.ir2, masihi-s@ajums.ac.ir3, e.farhadi67@yahoo.com4, sadeghimahsa117@gmail.com

ABSTRACT

Introduction: Trophoblast invasion into the decidual and decidual vessels is vital for placentation. Placental deficiencies relate to preeclampsia, fetal growth restriction (FGR) and small for gestational age (SGA) neonates. Prediction of major vascular events during pregnancy is feasible through uterine artery Doppler. The current study aimed to assess uterine artery Doppler disorder and its association with demographic characteristics of patients referring for first trimester screening.

Materials and Methods: The study population encompassed pregnant women referring for first trimester screening to Imam Khomeini Hospital in Ahvaz. To gather data, patients first completed a checklist, then underwent sonography and nuchal translucency (NT) thickness was determined. Subsequently, bilateral uterine artery Doppler was measured and recorded in the checklist.

Results: In this study, the mean uterine artery pulsatility index (PI) in the first trimester was 1.61. The mean age was 30.45 years with a standard deviation of 6.03, the mean weight was 71.15 kg with a standard deviation of 60.3, the mean height was 1.62 with a standard deviation of 0.07. Furthermore, the mean BMI was 27.04 with a standard deviation of 10.43. In the current study, in terms of determining obstetric history in patients referring for first trimester screening, primigravida had the highest frequency with 108 cases (36 percent). In the present study, no significant association was observed between uterine artery Doppler disorder and pregnancy outcomes including preterm delivery and IUGR ($p>0.05$), however a significant association was seen between uterine artery Doppler disorder and IVF ($p=0.001$).

Conclusion: In this study, no significant association was found between uterine artery Doppler examination in the first trimester and demographic characteristics of the patients,but this issue does not diminish the value of uterine artery examination ,and it seems that it is better to perform uterine artery doppler examination in the second trimester. yet a significant association was observed between uterine artery Doppler disorder and IVF. This indicates that uterine artery Doppler can be effective in predicting different pregnancy outcomes in the first trimester. Further adequate prospective studies utilizing standardized methods are required in the future to evaluate parameter selection and strategies for an associative aim to attain optimal prediction modalities. Advancing the knowledge of pathogenesis of complications during pregnancy facilitates the development of novel predictive and preventive modalities.

Keywords: Doppler ultrasonography; First trimester of pregnancy; Pregnancy-induced hypertension; Uterine artery.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

A. Introduction and Statement of the Problem

One of the imaging modalities that has assisted clinicians in recent years for fetal health assessment, alongside various clinical and laboratory tests, is conventional and color Doppler ultrasonography. In color Doppler ultrasonography, the phenomenon of Doppler is utilized. This physical principle was first defined by Christian Doppler about 150 years ago and refers to the change in frequency or wavelength due to motion; this motion can be in the wave generator, receiver, or reflector (1). In medicine, the origin of Doppler is motion, specifically blood flow. In arteries, each cycle created by cardiac activity generates a wave that begins with systole and ends with diastole. Various hemodynamic factors in different body vessels produce different curves with variable pulsatility, which can be low, medium, or high. Uteroplacental blood flow can be examined through Doppler ultrasonography, which is a noninvasive method. The impedance of uterine artery blood flow progressively decreases in the first and second trimesters of normal pregnancy, attributed to trophoblastic invasion into the myogenic-elastic coating of the spiral uterine arteries (2).

Hemorrhage, infection, and pregnancy-induced hypertension are among the most important causes of maternal mortality during pregnancy. Recent studies have shown that increased resistance in uterine vessels is associated with an elevated risk of progression toward preeclampsia and intrauterine growth restriction. Preeclampsia increases the complications of pregnancy and maternal, fetal, and neonatal mortality and remains one of the most significant unresolved issues in obstetrics. Despite extensive research, how it is initiated or exacerbated by pregnancy is unclear, and preventing its occurrence seems impossible (3).

One of the primary aims in fetomaternal medicine is early diagnosis of high-risk cases so that appropriate interventions can be implemented to improve maternal and fetal outcomes.Sheibani and colleague In a historical cohort study on 8460 cosecutive pregnant women recruited for chromosomal abnormalities screening within the first trimester at fertility infertility and perinatology research center in ahvaz joundishapor of medical sciences between april 2014 and 2015 showed that measuring the serum level of MOM papp-A during first trimester can be a valuable marker for predicting adverse outcome of pregnancy such as SGA and abortion .the best cutoff value for this marker to predict outcome is 0.3 in pregnant Iranian women.(4) Thus far, no study in Iran has determined the demographic characteristics of patients with uterine artery Doppler parameters in high-risk pregnancies, and most studies have focused on some Doppler indices and their association with preeclampsia and IUGR. Moreover, uterine artery Doppler measurement is not a routine intervention in pregnancy (5). In the present study, we investigate the association between factors like obstetric history or NT thickness and abnormal uterine artery Doppler to determine if a significant correlation exists between uterine artery Doppler disorder and maternal demographic characteristics. This could guide pregnant women referring for first trimester screening, so that in the presence of risk factors, they undergo uterine artery Doppler evaluation from the beginning, and necessary interventions and follow-ups are conducted to improve maternal and fetal status.

B. Materials and Methods

This cross-sectional study was conducted at Imam Khomeini Hospital in Ahvaz. The study population included pregnant women referring for first trimester screening at Imam Khomeini Hospital in Ahvaz. The inclusion criteria were pregnant women referring for first trimester screening at Imam Khomeini Hospital. Data on pregnant women was collected by the researcher based on a checklist. To gather data, patients first completed the prepared checklist, then underwent sonography and NT thickness was determined. Subsequently, bilateral uterine artery Doppler was measured and recorded in the checklist.

Ethical Considerations

This study was approved by the Ethics Committee of Ahvaz Jondishapur University of Medical Sciences. The Ethics Committee of Ahvaz Jondishapur University of Medical Sciences accepted all study protocols (IR.AJUMS.HGOLESTAN.REC.1401.128). Accordingly, before any intervention, written informed consent was obtained from all participants. This study was part of the thesis of resident Mahsa Sadeghi.

Findings

Of the total 300 subjects, the mean age was 30.45 years with a standard deviation of 6.03, the mean weight was 71.15 kg with a standard deviation of 60.3, the mean height was 1.62 meters with a standard deviation of 0.07. Also, the mean BMI was 27.04 with a standard deviation of 10.43. There were 108 (36%) primigravida, 80 (26%) second gravida, 75 (24%) third gravida, 21 (7%) fourth gravida, 6 (2%) fifth gravida, 7 (2.3%) sixth gravida, and 3 (2.7%) seventh gravida. The mean PI-UtA was 1.61 with a standard deviation of 0.55; the minimum PI-UtA was 0.45 and the maximum was 2.99. The mean Right_PI was 1.61, the mean Left_PI was 1.66, and the mean PI was 0.55. (Table 1) There were 18 (6%) twin pregnancies and 282 (94%) singleton pregnancies. 260 (86%) had no underlying disease, 11 (3.6%) had diabetes, 15 (5%) had hypertension, and 14 (4.6%) had other underlying diseases. 13 (4.3%) had diabetes and 12 (4%) had hypertension in a previous pregnancy. Among those with abnormal Doppler, no one had a history of IUGR, while 1 (100%) person with normal Doppler had a history of IUGR. There was no significant association between history of IUGR neonates and abnormal Doppler. (Table 2) Of those with

abnormal Doppler, 5 (10.4%) conceived through IVF and 67 (34.7%) conceived without IVF. Of those with normal Doppler, 43 (89.6%) conceived through IVF and 126 (65.3%) conceived without IVF. There was a significant association between abnormal Doppler and IVF. (Table 4)

Table 1. Determining descriptive indices in Right_PI, Left_PI, and Average_PI variables

variable	Average	standard deviation	min	max
Right_PI	1.61	0.86	0.43	11.40
Left_PI	1.66	0.64	0.00	3.08
Average_PI	1.61	0.55	0.45	2.99
PI-UtA (index pulsatility artery uterine)	1.61	0.55	0.45	2.99

Table 2. Determining history of IUGR neonates in patients referring for first trimester screening

Variable	Category	Frequency (Percent)	Frequency (Percent)	P-value
		History of IUGR		
		Yes	No	
Abnormal Doppler	Yes	0 (0)	40 (32)	0.49
	No	1(100)	85 (68)	

Table 3. Frequency of twin pregnancy, underlying disease, and history of disease in previous pregnancy

Variable	Frequency	Frequency (Percent)
Twin pregnancy		
Yes	18	6
No	282	94
Underlying disease		
None	260	86
Diabetes	11	3.6
Hypertension	15	5
Other	14	4.6
History of disease in previous pregnancy		
Gestational diabetes	13	4.3
Gestational hypertension	12	4

Table 4. Determining use of IVF fertility treatments in patients referring for first trimester screening

Variable	Category	Frequency (Percent)	Frequency (Percent)	P-value
		Use of IVF fertility treatments		
		Yes	No	
Abnormal	Yes	5 (10.4)	67 (34.7)	
Doppler	No	43 (89.6)	126 (65.3)	

A. Discussion

The present study investigated uterine artery Doppler disorder and its association with demographic characteristics of patients referring for first trimester pregnancy screening. In this study, the mean uterine artery PI in the first trimester was 1.61. The mean age was 30.45 years with a standard deviation of 6.03, the mean weight was 71.15 kg with a standard deviation of 60.3, the mean height was 1.62 with a standard deviation of 0.07. Also, the mean BMI was 27.04 with a standard deviation of 10.43. In the present study, in terms of determining obstetric history in patients referring for first trimester screening, primigravida had the highest frequency with 108 cases (36 percent). In this study of 282 (94 percent) and 18 (6 percent) patients were singleton and twin pregnancies, respectively. Regarding underlying disease, 260 (86 percent) had no underlying disease, 11 (3.6 percent) had diabetes, 15 (5 percent) had hypertension, and 14 (4.6 percent) had other underlying diseases.

The study by Oancea et al. (Romania, 2020) (1) on uterine artery Doppler for first trimester prediction of preeclampsia in 120 high-risk patients found that most individuals, 94 (78.33%), had normal blood pressure, and regarding BMI, most individuals, 100 (83.33%), had a BMI under 30. Also in this study, 90 (75%) were over 37 weeks gestation at birth. Regarding age, most individuals, 60 (50%), were between 30-40 years old. They showed in this study that out of 120 pregnant participants, 26 (21.6%) developed preeclampsia during pregnancy, such that the presence of vascular disorder before pregnancy or unexplained adverse obstetric events at their time increases the risk of

preeclampsia. Patients with high uterine artery PI and bilateral notching in the first trimester had the highest risk of developing preeclampsia. They reported that in preeclampsia screening, in high-risk patients, performing uterine artery Doppler exam between 11-14 weeks of gestation provides diagnosis of pregnancies with increased preeclampsia risk progression with 61.5% sensitivity and 63.8% specificity based on PI analysis. Also, if adding bilateral notching to this parameter, the predictive power increases slightly (sensitivity = 65.4%, specificity = 66%).

In the study by Scandiuzzi et al. (2016) in Brazil on 162 low-risk singleton pregnant mothers undergoing routine antenatal care, the mean UtA PI greater than 2.15 in the first trimester was considered abnormal.

The present study showed that among those with abnormal Doppler, no one had a history of IUGR, while 1 (100%) person with normal Doppler had a history of IUGR. However, there was no significant association between history of IUGR neonates and abnormal Doppler (p=0.49). In normal pregnancy, the spiral arteries in the placental bed are invaded by trophoblasts, which incorporate into the vessel wall and replace the endothelium, muscular and elastic layers, and neural tissues. These physiological changes transform the spiral arteries from narrow muscular vessels into dilated, non-muscular channels independent of maternal vasomotor control. In placental dysfunction, trophoblastic invasion of the spiral arteries is impaired, and this defect is most pronounced in preeclampsia and IUGR. Indirect evidence of impaired placental perfusion in pregnancies destined to develop preeclampsia and IUGR has been provided by studies of Doppler in the uterine arteries, showing increased PI throughout the second trimester and also in the first trimester (2). The ideal and acceptable biomarker for preeclampsia and IUGR should be easily measured, simple, fast, noninvasive, inexpensive, straightforward to perform, and should not expose the patient to discomfort or risk. This technology should be widely available and have reproducible, reliable results with good sensitivity and specificity. Ideally, it should provide an opportunity to intervene to prevent disease progression or at least lead to better maternal and/or fetal outcomes, should distinguish between mild versus severe preeclampsia and IUGR, should identify risk early in pregnancy and optimally in the first trimester, and should act as an acceptable mediator in its pathogenesis (3).

In the first trimester, the use of uterine artery Doppler alone for predicting hypertensive disorders of pregnancy is limited, and other indices should be considered for combining with uterine artery Doppler. In one prospective study, uterine artery blood flow was examined in 405 pregnant women at 13+6-11 weeks, and no significant difference in UtA-PI and presence of uterine artery notching was found between pregnant women who later developed preeclampsia and women without preeclampsia (6). Moreover, a large sample study on 8,061 pregnant women showed that the lowest UtA-PI of pregnant women who later developed preeclampsia was significantly higher than the normal pregnancy outcomes (5). Meanwhile, some researchers emphasized that a single UtA-PI value cannot accurately reflect uterine artery resistance, so they recommended using the mean PI in multiples of the median (MoM) after adjusting the raw maternal data (7). Notably, regarding screening patients with late-onset placental-related diseases, UtA-PI detection in the third trimester was better than first trimester, as they increased with gestational age rather than in the first trimester (7). Overall, changes in uterine artery blood flow from first trimester to second trimester were related to hypertensive disorders of pregnancy and FGR (8).

Abnormal placentation (abnormal uterine artery Doppler) may potentially cause stillbirth, and reasonable intervention before birth and timely treatment could help reduce stillbirth. In contrast, the sensitivity of uterine artery Doppler alone in predicting stillbirth in the first trimester was only 14.5% (8).

In the present study, of those with abnormal Doppler, 2 (20%) had a history of preterm delivery in a previous pregnancy, while 60 (32.8%) did not have a history of preterm delivery in a previous pregnancy. Of those with normal Doppler, 8 (80%) had a history of preterm delivery in a previous pregnancy, while 123 (67.2%) did not have a history of preterm delivery in a previous pregnancy. There was no significant association between abnormal Doppler and history of preterm delivery in a previous pregnancy (p=0.39). According to recent studies, abnormal placentation and decreased uterine artery blood flow are associated with preterm delivery (10). Given the association between UtA-PI and spontaneous preterm delivery in the second trimester, UtA-PI was higher in patients who delivered before 33 weeks compared to those delivering at 33 weeks or later (7S). The increased UtA-PI in patients with spontaneous preterm delivery may be the result of impaired placental function, as histopathological findings have shown that spiral artery remodeling was insufficient in these patients (11).

Also in the present study, of those with abnormal Doppler, 5 (10.4%) conceived through IVF and 67 (34.7%) conceived without IVF. Of those with normal Doppler, 43 (89.6%) conceived through IVF and 126 (65.3%) conceived without IVF. There was a significant association between abnormal Doppler and IVF (p=0.001). The increased adverse pregnancy outcomes following IVF compared to natural conception have been extensively studied, most importantly placenta-related complications such as: placental implantation abnormalities (placenta previa, placenta accreta, placental infarcts) and short-term and long-term placental insufficiency. The reported associated diseases. Also, differences in maternal characteristics and IVF methods used could explain the apparent paradoxical decrease in UtA-PI in the eFET group during pregnancy, which is known to have a higher incidence of early-onset preeclampsia (12). Instead, the higher risk of LGA and lower risk of SGA could be explained by the lower UtA-PI in eFET. Rizzo et al. observed no difference in UtA-PI between frozen-thawed ET, fresh ET (13). Overall, the reasons for the difference in UtA-PI values in the first trimester in different studies and the association or lack of association between uterine artery Doppler and various pregnancy outcomes could be due to differences in sample size,

UtA-PI measurement at different pregnancy percentiles, and at different weeks in the first trimester. The limitations of the present study include small sample size, lack of evaluation of sensitivity, specificity and PI-UtA cut-off value in predicting various pregnancy complications, unknown PI-UtA value at different pregnancy percentiles in the first trimester, and lack of investigation of the association between uterine artery Doppler disorder and other pregnancy outcomes.

B. Conclusion

Early diagnosis of high-risk pregnancies prone to various adverse outcomes allows the use of preventive treatment. Using uterine artery Doppler and examining its association with different pregnancy outcomes can identify pregnancies that cause severe complications. In the present study, no significant association was observed between uterine artery Doppler disorder and demographic characteristics of the patients, but this issue does not diminish the value of uterine artery examination ,and it seems that it is better to perform uterine artery doppler examination in the second trimester.yet a significant association was seen between uterine artery Doppler disorder and IVF. This indicates that uterine artery Doppler can be effective in predicting different pregnancy outcomes in the first trimester. Using first trimester biomarkers and uterine artery Doppler indices has the greatest potential to become a screening method in low-resource settings. Further adequate prospective studies utilizing standardized methods are required in the future to evaluate parameter selection and strategies for an associative aim to attain optimal prediction modalities. Advancing the knowledge of pathogenesis of complications during pregnancy facilitates the development of new prediction and prevention modalities.

Acknowledgments: I don't have

Conflict of interest: I don't have

Financial support: I don't have

Ethics statement: I don't have

References:

1. Oancea M, Grigore M, Ciortea R, Diculescu D, Bodean D, Bucuri C, et al. Uterine artery doppler ultrasonography for first trimester prediction of preeclampsia in individuals at risk from low-resource settings. Medicina. 2020;56(9):428.

2. Visintin C, Mugglestone MA, Almerie MQ, Nherera LM, James D, Walkinshaw S. Management of hypertensive disorders during pregnancy: summary of NICE guidance. Bmj. 2010;341.

3.Roberts J, Cooper DW. Pathogenesis and genetics of pre-eclampsia. The Lancet. 2001;357(9249):53-6

.

4.Mohamadjafari R , Masihi S , Baraty MMaraghi E, Sheibani S,Sheikhvatan M. Value of pregnancy-associated plasma protein –A (ppap-A) for predicting adverse pregnancy outcome : Archive of Irnin Medicine October 2019;22(10) 584-587.

5.Poon LC, Stratieva V, Piras S, Piri S, Nicolaides KH. Hypertensive disorders in pregnancy: combined screening by uterine artery Doppler, blood pressure and serum PAPP-A at 11–13 weeks. Prenatal Diagnosis: Published in Affiliation With the International Society for Prenatal Diagnosis. 2010;30(3):216-23.

6. Prakansamut N, Phupong V. Serum SHARP1 and uterine artery Doppler for the prediction of preeclampsia. Scientific reports. 2019;9(1):12266.

7. Llurba E, Turan O, Kasdaglis T, Harman CR, Baschat AA. Emergence of late-onset placental dysfunction: relationship to the change in uterine artery blood flow resistance between the first and third trimesters. American journal of perinatology. 2012:505-12.

8. Gomez O, Figueras F, Martinez J, Del Rio M, Palacio M, Eixarch E, et al. Sequential changes in uterine artery blood flow pattern between the first and second trimesters of gestation in relation to pregnancy outcome. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2006;28(6):802-8.

9. Fouron JC, Absi F, Skoll A, Proulx F, Gosselin J. Changes in flow velocity patterns of the superior and inferior venae cavae during placental circulatory insufficiency. Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2003;21(1):53-6.

10. Parra-Cordero M, Sepúlveda-Martínez A, Rencoret G, Valdés E, Pedraza D, Muñoz H. Is there a role for cervical assessment and uterine artery Doppler in the first trimester of pregnancy as a screening test for spontaneous preterm delivery? Ultrasound in Obstetrics & Gynecology. 2014;43(3):291-6.

11. Kim YM, Bujold E, Chaiworapongsa T, Gomez R, Yoon BH, Thaler HT, et al. Failure of physiologic transformation of the spiral arteries in patients with preterm labor and intact membranes. American journal of obstetrics and gynecology. 2003;189(4):1063-9.

12. Perry H, Lehmann H, Mantovani E, Thilaganathan B, Khalil A. Correlation between central and uterine hemodynamics in hypertensive disorders of pregnancy. Ultrasound in Obstetrics & Gynecology. 2019;54(1):58-63.

13 .M. Rizzo G, Aiello E, Pietrolucci ME, Arduini D. Are there differences in placental volume and uterine artery Doppler in pregnancies resulting from the transfer of fresh versus frozen-thawed embryos through in vitro fertilization. Reproductive sciences. 2016;23(10):1381-6.