Value of 3D Ultrasonographic Assessment of Placental Volume and Perfusion Indices in The First Trimester As Predictors to The Occurrence of Preeclampsia

Original Article

Shaimaa Belal[1], Manal Abdel-Wanees Al-sayed[2], Hany Mahmoud Abd El Hamid[2], Ashraf elbaz[3]

Department of Obstetrics and Gynecology, [1]Faculty of Medicine, Helwan University, [2]Al-Sahel Teaching Hospital, [3]Al-Gala Teaching Hospital, Cairo, Egypt

ABSTRACT

Aim: The purpose of this study is to determine placental volume and vascular flow indices during the first trimester and their values as predictors of developing preeclampsia.

Materials and Methods: A prospective analysis for standard antenatal follow up at 11 to 13 weeks of gestation was performed on 177 singleton pregnant women visiting the antenatal care outpatient clinic at Al-Sahel Teaching Hospital between June 2018 and June 2019. Transabdominal 3D ultrasonography ('placental biopsy') to determine placental volume and power Doppler assessment of placental vascularization were done for all cases.

Results: Comparative analysis of placental volumes between the normal pregnancy and preeclamptic pregnancies groups revealed a statistically high significant difference (*P value < 0.001*). The mean volume in the two groups was 84.9 ± 22 and 45.6 ± 11.4 cm3, respectively. In the normal pregnancy group, the volume of placenta was larger than preeclamptic pregnancies group. Also, comparative analysis of placental vascularization index (VI), flow index (FI), and vascularization flow index (VFI) between the normal pregnancy group and pregnancies group that developed preeclampsia revealed a statistically high significant difference (*P value <0.001*). The mean values of (VI), (FI), and (VFI) in the two groups were (24.7±8.1, 95.4±9.1, 13.1±3. 7) and (16.2±5.8, 54.6±10.9, 8.1±2.1) respectively.

Conclusion: Quantitative assessment of placental volume and vasculature using 3D power doppler VOCAL TM techniques can be used in the 1st trimester to predict preeclampsia. Placentas of pregnancy complicated with preeclampsia have smaller volume, fewer blood vessels (reduced VI) and decreased blood flow (reduced FI).

Key Words: Placental indices, Preeclampsia, 3D U/S

Received: 21 January 2022, **Accepted:** 18 March 2022

Corresponding Author: Shaimaa Belal, Department of Obstetrics and Gynecology, Faculty of Medicine, Helwan University, Cairo, Egypt, **Tel.:** 01090650463, **E-mail:** drshimaa444@gmail.com

ISSN: 2090-7265, May 2022, Vol.12, No. 2

INTRODUCTION

Maternal background and risk factors alone, particularly in nulliparal, might not be predicting the initiation of preeclampsia. Improving preeclampsia diagnosis has therefore become the subject of a large amount of research[1,2].

Advances in both ultrasound and understanding of preeclampsia's pathophysiology have renewed efforts to find an early diagnostic tool for this condition through screening system performed in the first trimester.

There have also been several efforts to distinguish between high and low risk pregnancies in the first trimester. Mean calculation of arterial blood pressure and the knowledge of the pathophysiology of preeclampsia have revived attempts at finding a screening method for the disorder with the focus shifted to identifying a screening program for the first trimester[3].

A fascinating feature may be a direct assessment of trophoblastic invasion since it is strongly linked to preeclampsia growth. The advent of 3-dimensional (3D) ultrasound technology, with the choice of measuring vascular volumes, provided an excellent opportunity to research early improvements in utero-placental circulation space (UPCS), which involves mother's spiral arteries and the inter-villous space[4,5].

AIM OF THE STUDY

This work aimed to assess the value of 3D-placental volume and vascular flow indices as predictors of preeclampsia in the first trimester.

 DOI:10.21608/ebwhj.2022.117548.1166

PATIENTS AND METHODS

A prospective cohort study included 177 pregnant women attended the antenatal care outpatient clinic in Al-Sahel Teaching Hospital between June 2018 and June 2019 for routine antenatal care at 11 to 13 weeks of gestation.

Inclusion criteria included women with singleton pregnancy (11 and 13 weeks) and exclusion criteria included pregnant multifetal and malformations of the embryo.

Ethical consideration: well, informed written consent has been taken from all women included in the study. All women included were subjected to; complete history taking, full examination, 2D ultrasound scanning, Doppler assessment of uterine artery, assessment of placental volume and assessment of placental vascular indices.

Blood flow in the placenta was examined using 3D power Doppler technique. The whole placenta was put inside the region of interest the power Doppler was applied to the whole placenta then a 3D volume of the power Doppler is acquired, and a volume histogram was obtained after accepting the region of interest then automatically calculate the values of VI, FI and VFI for the entire placental volume. Follow up: All cases were followed up regularly until delivery. The primary outcome data were whether patients developed preeclampsia or not.

STATISTICAL ANALYSIS

All statistical calculations were done using computer programs Microsoft Excel 2013 and SPSS version 20.

RESULTS

This study included 177 women with single pregnancy during the first trimester. Out of them, 8 women had second-trimester spontaneous abortions before 24 weeks of gestation, and 7 patients were lost to follow-up. The remaining were 162 women. 22 of the 162 (13.61%) developed preeclampsia and 140 (86.41%) women did not. Among those with preeclampsia, 9 (40.91% of preeclampsia group) had severe preeclampsia and required delivery prior to 34 weeks. 2 patients with preeclampsia (9.11% of preeclampsia group) had a small-for gestational-age (SGA) fetus. So, all included women (n = 162) were subdivided into two groups; normal group included no preeclampsia developed (n = 140 cases= 86.4 percent). Affected group included preeclampsia developed (n = 22 cases = 13.6%).

The age distribution of studied women varied between the ages of 18 and 44 (Table 1). The number of obese women (BMI>30 kg / m2) was 127. The CRL ranged from 43.7 to 84 at the time of registration (Table 2), indicated that nulliparity and obesity were major risk factors for developing preeclampsia. The CRL was not different between two groups.

Preeclampsia is substantially correlated with Caesarian section. Of major risk factors for developing preeclampsia, history of previous preeclamptic pregnancy, hypertension and diabetes (Table 4).

Uterine Doppler PI and RI are substantially higher in preeclampsia (Table 5). The placental volume was slightly lower in preeclampsia than in normal pregnancies. In preeclamptic situations three D strength placenta Doppler indices were substantially lower. Regarding the mean index of uterine artery pulsatility (PI), it was showed that preeclamptic patients had substantially higher UADPI compared with controls. A quantitative examination of the placental volume between the usual pregnancy community and preeclamptic pregnancies showed a statistically important discrepancy (*P value < 0.001*) in the present case. In the two groups, the mean volume was 84.9±22.3 and 45.6±1.4 cm3, respectively. In the normal group of pregnancies, the placenta volume was greater than the group of preeclamptic pregnancies. A quantitative review of the placental vascularization index (VI), flow index (FI), and vascularization flow index (VFI) between the usual pregnancy group and preeclampsia group showed a statistically significant difference (*P value < 0.001*) with the mean values of (VI), (FI), and (VFI) were (24.7±8.1, 95.4±9.1, 13.1±3.7), and (16.2±5.8, 54.6±10.9, 8.1±2.1) respectively.

Table 1: Clinical profile of all studied women (n=162)

Clinical profile	Mean	Range
Age (y)	27.41±9.2	18-43
Parity	3.1±1.91	0-51
BMI (kg/m^2) obese>30 (Number, %)	31.91±10.71 127	18.1-43 39.2
SBP at time of enrollment	124±12.51	94-151
DBP at time of enrollment	88.61±7.451	70-111
CRL (mm)	63.11±13.71	43.7-85

Table 2: Clinical profile for each group (n=140), (n=22)

Clinical profile		Unaffected (140 women)	Affected (22 women)	*P*
Age (years)	Means	29.7113.41±	26.1112.11±	0.09
	Median	33	26	
	Range	18-44	18-38	
Parity	Nullipara n (%)	15(5.4)	9(20.51)	<0.001
	Multipara n (%)	265(94.61)	35(79.51)	
BMI	Mean± _SD Range	28.918.11±	33.4110.21±	<0.001
	obese>30 n (%)	18-35	23-44	
		94(33.61)	33(75.01)	<0.001
CRL (mm)	Mean± _SD range	63.41 ±13.71 43.71-84	6313.71± 50.51-79.71	NS

Table 3: Mode of delivery in the studied groups (n=162)

Mode of delivery	Normal	preeclampsia	*P*
VD n (%)	65(46.11)	5 (20.41)	<0.001
CS n (%)	76(53.91)	18 (79.61)	

Table 4: Risk factors for preeclampsia in all women (n=162)

Risk factors for preeclampsia	Un affected	Affected	*P*
Previous history of PE n (%)	8(5.41)	5(20.51)	0.02
history of hypertension n (%)	6(5.2)	6(25.1)	<0.001
History of DM n (%)	1(0.711)	2(6.81)	0.021
history of SLE n (%)	1(0.711)	0(0.0)	0.981
history of CKD n (%)	0(0.0)	1(1.41)	0.781
History of SCD n (%)	0(0.0)	1(1.41)	0.781

Table 5 a: Uterine artery Doppler study at the 1st trimester among studied groups (n=162)

Uterine artery	Un affected	Affected	*P*
PI -mean±SD	0.761±0.141	1.141±0.371	<0.001
-range	0.6-0.9	0.91-1.51	
RI -mean±SD	0.491±0.11	0.581±0.131	<0.001
-range	0.421-0.551	0.521-0.721	

Table 5 b: Ultrasonic placental examination at the 1st trimester among studied groups (n=162)

	Un affected	Affected	*P*
Lateral placenta (n, %)	56(40.0)	16(70.5)	0.01
mean±SD range	84.9122.31±	45.6111.41±	
	54.21-152.911	33.51-62.41	
mean±SD range	20.21± 5.31	19.81± 4.91	
	10.91-27	13.31-24.51	

Table (5 c): 3D power Doppler indices of placenta at the 1st trimester among studied groups (n=162)

3D power Doppler indices	Unaffected	affected
VI	24.71±8.11	16.21±5.81
FI	95.41±9.11	54.61±10.91
VFL	13.11±3.71	8.11±2.11

Table 6: Diagnostic value of 3D US parameters in prediction of PE (n=162)

Area Under the Curve					
Test Result Variable(s)	Are (2) a	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval Lower Bound	Upper Bound
VI	.750	.144	.150	.467	1.033
FI	.694	.157	.262	.387	1.001
VFI	.722	.169	.200	.390	1.054

The test result variable (s): VI, FI, VFI has at least one tie between the positive actual state group and the negative actual state group

Table 7: Diagnostic value of uterine artery Doppler and placental volume in prediction of PE (n=162)

	VI	FI	VFI
Cut off	<22.71	<51.31	<10.41
Sensitivity	81.31	86.41	88.61
Specificity	71.41	70.71	75.81
PPV	31.31	34.81	39.11
NPV	94.71	88.41	80.41
Accuracy	72.21	68.71	78.11
		VI+FI+VF	I+PV
Specificity		99.31	
Sensitivity		97.71	
NPV		99.61	
PPV		95.61	

Table (8): Predictive values of combined 3D vascular indices and placental volume in prediction of preeclampsia (n=177)

Predictive values	PI	RI	PV
Cut off	>0.90	>54	<50.7
Auc	0.941	0.71	0.11
Sensitivity	93.21	90.91	95.41
Specificity	92.61	91.71	94.61
Ppv	72.91	65.61	72.71
Npv	98.81	98.51	99.31

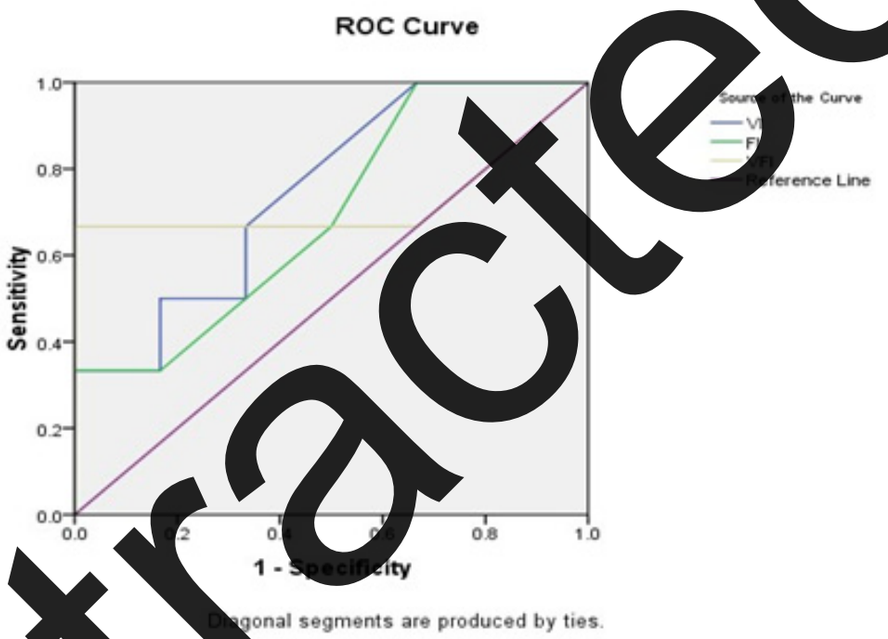

Fig. 1: The diagnostic value of the 3DUS parameters in the prediction of PE (n=162)

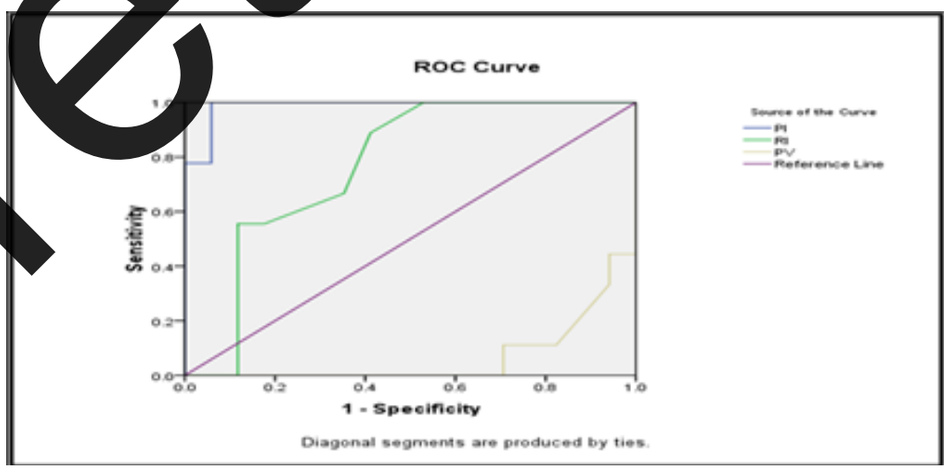

Fig. 2: Diagnostic value of uterine artery Doppler and placental volume in prediction of PE (n=162)

DISCUSSION

The placenta has a crucial function in pathogens of certain harmful effects in pregnancy. Impaired trophoblastic penetration of the maternal spiral arteries and their shift from small muscle vessels to broad non-vascular channels in the 2nd trimester is responsible for the faulty placement of PE[6]. The advent of 3-dimensional (3D) ultrasound technology with the possibility of measuring vascular volumes has provided an excellent opportunity to research early improvements in the area for utero-placental circulation (UPCS), which involves the maternal spiral arteries and inter-villous area. Vascular indices within the placenta are determined from voxel-formed three-dimensional data[7,8]. These indices are thought to reflect the number of blood vessels within the volume (VI), the intensity of flow at the time of the three-dimensional (3D) sweep (FI), and both blood flow and blood vessels number (VFI). Using these indices, 3D power Doppler attempts to identify the different branches of the villous vessels, as well as the quantitative assessment of the number of vessels. So, reduction in these indices has the potential of being an earlier marker of placental dysfunction than the increase in the uterine and umbilical artery resistance which occur later[9].

The purpose of this study is to check the hypothesis that as screening measure for preeclampsia, 3D-placental volume and vascular flow indices that be used during the first trimester.

At first, 177 patients were included. Of them 8 patients had second-trimester spontaneous abortions before 24 weeks of gestation and 7 patients were lost to follow-up. Of the remaining 162 patients, 22 (13.6%) developed preeclampsia and 140 (86.4%) patients did not. Among those with preeclampsia, 9 (40.9%) had severe preeclampsia. 5 of these had preeclampsia requiring delivery prior to 34 weeks.

Alae Eldeen *et al*., 2016 reported, who researched PE screening for the first trimester at Tanta University during the period June 2013 to December 2015. They found a prevalence of pregnant women who developed pre-eclampsia 14 among 266 women (5.26%), of whom 2 cases were early pre-eclampsia (14.3%) and 12 cases were late pre-eclampsia (85.7%)[10]. Many causes were well-documented as risk factors for pre-eclampsia, including prior preeclampsia, antiphospholipid syndrome, family history of pre-eclampsia, chronic kidney disorder, insulin-dependent diabetes, concurrent abortions, pre-existing hypertension and nulliparity[11]. With respect to the mean index of uterine artery pulstility (PI), the present study found that preeclamptic patients had significantly higher UADPI compared to control.

This is in line with the findings of Plasencia *et al*., 2007, which reported that uterine artery Doppler studies at 11-13 weeks showed that impedance to flow in pregnancies that subsequently develop hypertensive disorders and that the increase is particularly marked for early preeclampsia[12].

Khong *et al.* (2015) reported that the sensitivities and specificities of the Doppler uterine artery indices for predicting preeclampsia in low-risk populations range from 34 % to 76 % and 83 % to 93 % respectively. They stated that this test's low sensitivity limits its usefulness as an isolated disease marker[13].

In this study, a comparative analysis of placental volume between the normal pregnancy group and preeclamptic pregnancies revealed a statistically high significant difference (*P value <0.001*). The mean volume in the two groups was 84.9 ± 22 and 45.6 ±11.4 cm3, respectively. In the normal pregnancy group, the volume of placenta was larger than preeclamptic pregnancies group. In 2015, Hashish *et al.* published similar findings. They observed that there was a statistically important disparity in such births in the placental amount that formed PE relative to uninfected gestations (49.7 ± 31.6 vs. 91.8 ± 32.6, $p<0.001$)[14].

Odibo *et al.* (2011) demonstrated that the mean first-trimester placental volumes of these pregnancies that formed preeclampsia were not substantially different relative to uninfected gestations[15].

In this study, a quantitative review of the placental vascularization index (VI), flow index (FI), and vascularization flow index (VFI) between the normal pregnancy group and pregnancies with preeclampsia group showed a statistically important discrepancy (*P value < 0.001*). The mean values of (VI), (FI), and (VFI) were (24.7 ± 8.1, 95.4 ± 9.1, 13.1 ± 3.7) and (16.2 ± 5.8, 54.6 ± 10.9, 8.1 ± 2.1) respectively. These results clearly demonstrate that pregnancy placentas complicated with preeclampsia also have fewer blood vessels (reduced VI) and reduced blood flow (reduced FI). Our findings suggest that this ultrasonographic tool could predict preeclampsia development.

Unlike our research, Hannaford *et al*., (2015) identified no major variations in placental vascular indices in women developing preeclampsia[16].

CONCLUSION

Placentas in pregnancy affected by preeclampsia may have decreased volume, less blood vessels (reduced VI) and poorer blood pressure (reduced FI).

REFERENCES

1. Duley, L (2009): The global impact of preeclampsia and eclampsia. Semin. Perinatol, 33(3):130-

2. Parra-Cordero M, Rodrigo R, Barja P, Bosco C, Rencoret G, Sepúlveda-Martinez A & Quezada S (2013): Prediction of early and late pre-eclampsia from maternal characteristics, uterine artery Doppler and markers of vasculogenesis during first trimester of pregnancy. Ultrasound in Obstetrics & Gynecology, 41(5): 538-44.

3. Cnossen JS, Vollebregt KC, de Vrieze N, ter Riet G, Mol BW, Franx A, Khan KS and van der Post JA (2008): Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: systematic review and meta-analysis. BMJ, 336(7653):1117-20.

4. Pathak S, Hook E, Hackett G, Murdoch E, Sebire NJ, Jessop F & Lees C (2010): Cord coiling, umbilical cord insertion and placental shape in an unselected cohort delivering at term: relationship with common obstetric outcomes. Placenta, 31:963-8.

5. Khalil A, Cowans NJ, Spencer K, Goichman S, Meiri H & Harrington K (2009): First trimester maternal serum placental protein 13 for the prediction of pre-eclampsia in women with a priori high risk. Prenat Diagn, 29:781-9.

6. Kovo M, Schreiber L & Bar J (2013): Placental vascular pathology as a mechanism of disease in pregnancy complications. Thromb Res, 13 (supp1):518-21.

7. Zhong Y, Tuuli M & Odibo AO (2010): First-trimester assessment of placenta function and the prediction of preeclampsia and intrauterine growth restriction. Prenat Diagn, 30:293–308.

8. Kleinrouweler CE, Cheong-See FM, Collins GS, Kwee A, Thangaratinam S, Khan KS, Mol BWJ, Pajkrt E, Moons KGM & Schuit E (2016): Prognostic models in obstetrics: available, but far from applicable. American journal of obstetrics and gynecology, 214(1):79–90.

9. Guiot C, Gaglioti P, Oberto M, Piccoli E, Rosato R & Todros T (2008): Is three-dimensional power Doppler ultrasound useful in the assessment of placental perfusion in normal and growthrestricted pregnancies? Ultrasound Obstet Gynecol, 31:171-6.

10. Eldeen Y, Elkholi DG, Hefeda MAE and Nagy HM (2016): First Trimester Screening for Preeclampsia and Intrauterine Growth Restriction Using Uterine Artery Doppler and Maternal Serum Placental Growth Factor and Pregnancy Associated Plasma Protein- A. Reproductive Immunol Open Acc, 1:15

11. Poon LC, Kametas NA, Chelemen T, Leal A & Nicolaides KH (2010): Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. J Hum Hypertens, 4:104-10.

12. Plasencia W, Maiz N, Bonio S, Kaihura C & Nicolaides KH (2007): Uterine artery Doppler at 11+0 to 13+6 weeks in the prediction of preeclampsia. Ultrasound Obstet Gynecol, 30:742-9.

13. Khong SL, Kane SC, Brennecke SP & Costa FS (2015): First-Trimester Uterine Artery Doppler Analysis in the Prediction of Later Pregnancy Complications. Disease Markers, 2015:10.

14. Hashish N, Hassan A, El-Semary A, Gohar R & Youssef MA (2015): Could 3D placental volume and perfusion indices measured at 11-14 weeks predict occurrence of preeclampsia in high-risk pregnant women?. J Matern Fetal Neonatal Med, 28(9):1094-8.

15. Obido AO, Goetzinger KR, Huster KM, Christiansen JK, Obido L & Tuuli MG (2011): Placental volume and vascular flow assessed by 3D power Doppler and adverse pregnancy outcomes. Placenta, 32:230-4.

16. Hannaford KE, Tuuli M, Goetzinger KR, Odibo L, Cahill AG, Macones G & Odibo AO (2015): First-trimester 3-dimensional power Doppler placental vascularization indices from the whole placenta versus the placental bed to predict preeclampsia: does pregnancy-associated plasma protein a or uterine artery Doppler sonography help?. J Ultrasound Med, 34(6):965-70.