Evaluation The Role of Placental Volume, Vasculature In Predicting Pregnancies Complicated By Pre-Eclampsia and Intra Uterine Growth Restriction

Mohamed Ibrahim El-Tolemy [1,*] MSc, Ehab Hasanin Mohammed [1] MD,

Abdelmonsef Abdelhamed sedik [1] MD

Corresponding Author:

Mohamed Ibrahim El-Tolemy

tolemy1206@gmail.com

[1] Obstetrics and Gynecology Department, Military Production Medical Centre, Egypt.

[2] Obstetrics and Gynecology Department, Faculty of Medicine, Al-Azhar University Cairo, Egypt.

ABSTRACT

Background: Preeclampsia and Intrauterine growth restriction are major complication of pregnancy. Early and Non-invasive Ultrasound prediction of these conditions could be beneficial in early prevention and management.

Aim of the work: This study investigates if the placental volume and vasculature by Doppler (3DPD) can be dependible in predicting pregnancies complicated by Pre-eclampsia and/ or IUGR and normal pregnancies.

Patients and methods: This study was conducted on 150 pregnant women attending to antenatal clinic in Al azhar maternity hospital. We measured the placental volume and vascular indices.

Results: The study found that IUGR and/or preeclampsia were established in twenty cases. The cut-off level was determined according to the placental volume and vascular indices. The specificity, sensitivity, positive and negative predictive values of placental volume for prediction of IUGR and/or preeclampsia were found to be 80.4%, 68.5%, 52.1% and 86.8%, respectively. The specificity, sensitivity, positive and negative predictive values of placental flow index for prediction of IUGR and/or preeclampsia were found to be 68.9%, 78.3%, 40.2% and 88.5%, respectively.

Conclusion: The quantitative assessment of first trimester placental vasculature and placental volume can be considered a promising modality for early prediction of IUGR and/or PET. More researches of placental volume and vasculature for predicting preeclampsia and/or Intra Uterine Growth Restriction should be conducted on a large number of cases are necessary to further evaluate these parameters and strategies of combination with other modalities to achieve the best predictive models for preeclampsia and IUGR.

Keywords: *Preeclampsia; first trimester; intrauterine growth restriction; placental volume.*

INTRODUCTION

Preeclampsia and eclampsia are considered one of the main reasons for maternal and perinatal morbidity and mortality of all pregnancies worldwide, leading to 12–15% of direct maternal deaths.[1]

The prevalence of preeclampsia is about 2-10%, based on the studied population; and definition of preeclampsia and in addition, age less than 20 years are markedly affected. [2]

The impairment of uteroplacental circulation leads to poor obstetric outcomes as a result of i\nadequate placentation. This impairment leads to faulty invasion of trophoblastic and inadequate vascular response, intrauterine fetal growth restriction and preeclampsia. [3]

Doppler sonography has been utilized in different areas of obstetrics and gynecology to assess vascular indices in certain areas. This technique is considered a noninvasive method to assess the placenta during the first trimester and is used to assess the placental blood flow. Despite, the placenta has the main contribution in the development of preeclampsia, especially the defective invasion of trophoblastic cells and alteration of spiral arteries of the mother, According to this fact, assessment of placental vascular indices participates in determining pregnancies at risk for developing preeclampsia.[4]

Invasion of extra-villous trophoblast cells produces modifications at the end of the spiral arteries associated with the development of wide vascular mesh inside the myometrium beneath the basal plate of the placenta. A functional anatomical arteriovenous shunt was found in the subplacental part of the myometrium during pregnancy, and has a major contribution in gas exchange. [5]

Placental villi were protected by the effect occurred in maternal haemodynamics and may also feed the intervillous space by dissolved oxygen reservoir when blood flow is decreased temporally. Therefore, the formation of this rich vascular mesh in the myometrium is an important part of normal fetal growth and development of pregnancy. [6]

Increased uterine artery pulsatility index (PI) could be a sign of defective placental perfusion, which is related to the occurrence of PE/IUGR. Sonographer experience affects the indices of the uterine artery PI. In addition, preexisting diabetes mellitus, gestational age, racial   origin and maternal weight also affects the uterine artery PI.[7]

Preeclampsia can be either placental, maternal or both. When maternal microvasculardisease interact with normal placenta or poor implantation is found, this leads to Maternal PET. Before 20 weeks gestation (In the pre-clinical phase), there is decreased capacity of utero-placental circulation while during the clinical phase the placenta develops more hypoxia. In the more severe cases, (mostly of early-onset, i.e. prior to 34 weeks gestation), stillbirth can occur as well as fetal hypoxia. Maternal diseases involving the placenta or primary placental pathology can lead to IUGR. Marked placental pathology as pre-eclampsia related changes can be found in most of the cases of IUGR.[8]

One of the leading causes to perinatal morbidity and mortality is preeclampsia and intrauterine growth restriction (IUGR). Prenatal detection rates could be enhanced by early detection of women at risk of preeclampsia or IUGR occurrence which results in decreasing perinatal mortality allowing appropriate implementation of surveillance measures. [9]

Inadequate invasion of the endovascular trophoblast during the first trimester leads to the occurrence of both conditios. The clinical signs of these disorders show up during the second and third trimesters. [10]

A correlation between fetal birth weight and placental weight at the time of delivery has been   settled. In addition, a placental weight beneath the 10th percentile for gestational age is found associated with IUGR and preeclampsia affecting pregnancy. Recently, decreased birth weight and other poor obstetric results from variety of gross morphologic characteristics of placental. Sonographic. Prenatal placental evaluation is found to be an early detector of adverse pregnancy outcomes as a result of these observations. PE and IUGR are associated with the assessment of placental volume during the first trimester using 3-dimensional (3D) sonography. [11]

Assessment of intraplacental blood circulation using doppler examinations is found to be an effective way for fetal intrauterine growth restriction (IUGR) diagnosis and management especially because the changes in the placental vascular mesh results from the changes in values of fetal Doppler (i.e., umbilical artery) and of maternal Doppler (i.e., uterine artery). [6]

VOCAL technique and 3D Power Doppler are now available to assess the placental volume and intraplacental blood circulation. Three vascular indices could illustrate the Intra-placental blood circulation: flow index (FI), vascularization index (VI), and vascularization flow index (VFI). Vascularization index is the relation between the number of color voxels and the whole number of voxels in the sampled tissue, so it detects the amount of vascularized tissue.[12]

Flow index is the mean color value of whole color voxels and it determines the mean flow velocity in the sampled tissue. The vascularization-flow index is the mean color value of whole color and gray voxels and illustrates both: the blood flow and the vascularization. [13]

PATIENTS AND METHODS

Subjects: This study is a prospective randomized study on pregnant women between $(11 - 13^{+6})$ weeks gestation. Study period: june 2017 till june 2020.

Placental volume by 3D ultrasonography and vasculature indices study is done by VOCAL Technique.

Follow up of pregnant women in the study in second and third trimester for developing preeclampsia and/or intra uterine growth restriction.

It has been conducted at Al-Azhar Maternity University Hospital.

It included (150) women whom admitted to Antenatal care.

The criteria fulfilled by the selected patients: Pregnant women with single fetus with any presentation. Women sure of date of last menstrual period with regular cycles. Lack of systemic disease. Good visualization of the placenta.

Exclusion Criteria: Multiple gestation. Fetuses with congenital malformations. Women with any systemic disorder.

This prospective observational study took place at the Obstetrics and Gynecology department, Faculty of Medicine, Al Azhar University between June 2017 till June 2020. All the participating women were informed about the study and gave their consent before any procedure

Pregnant singleton women within 11 to 13^{+6} weeks of gestation based on the last menses were involved in the study. Women with chromosomal or structural abnormalities are eliminated from the study.

Diagnosis of IUGR and/or preeclampsia was the goal. Preeclampsia was described as a blood pressure at the minimum of 140/90 mmHg, measured on two different times six hours apart, accompanied by proteinuria at the minimum of 300 mg/24 h or at least 1+ using urine dipstick test or UPCI 0.3. After 20 weeks of gestation the increase in blood pressure and occurrence of proteinuria takes place for the first time. [14] Early onset preeclampsia was described as a preeclampsia that took place prior to the gestational age of 34 weeks. Late onset preeclampsia was described aspreeclampsia that took place at 34 weeks gestational weeks or later on. [15] IUGR was described as a fetal weight below the 10th percentile of gestation.[16]

The maternal demographic data, maternal and neonatal outcomes and placental volume were documented.

3DUS placental assessment was done using 4–8 MHz transducer real-time scanning. To regularize the acquisition procedures that was used to obtain 3D placental vascular indices, the settings for power Doppler were as follows: angiomode, cent; smooth, 4/5; FRQ, low;density, 6; filter, 2; quality, 16;actual power, 2dB; enhance, 16; balance, GO150; and pulse repetition frequency, 0.9.Images were obtained with the lowest possible gain, permitting us to achieve a good image of the placental vascular mesh while evading artifacts. The whole placental image was conducted using 2D ultrasound. To view the placental segments found posteriorly and laterally, the transducer was put at a fine lateral Inclination to achieve better view. To minimize any interference from beam shadowing resulting from the fetus lie, the transducer was finely rotated and a higher sweep angle 90^0 was used to obtain most of the longitudinal axis of the placenta.

After viewing the zone of clinical importance, placental volume was assessed using the VOCAL rotational technique and VOCAL software (3D SonoView, GE Medical Systems, Milwaukee, WI, USA). This technique comprises constantly defining the figure of the placenta after revolving the image of the placental six times in 30° increments.

Another analysis is done using VOCALt Software (3D SonoView, GE Medical Systems,Milwaukee, WI, USA) following the end of a full rotation, which measures placental volume,vascularization index (VI), flow index (FI) and vascularization flow index (VFI) automatically.

Statistical analysis

Analysis of the recorded data was done by using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were described as mean ± standard deviation (SD). Qualitative data were described as percentage and frequency. Data was explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test.

RESULTS

Initially,150 pregnant women undergoing screening in their first-trimester were involved in the study and follow up was performed along pregnancy and later on after delivery. 3 cases were eliminated due to miscarriage, and another 6 cases didn't show up for the follow-up. Amongthe remaining 141 pregnancies, 12 developed preeclampsia,5 developed IUGR ,3 allocated to Preeclampsia and IUGRr, while 121 pregnancies did not present this complications.
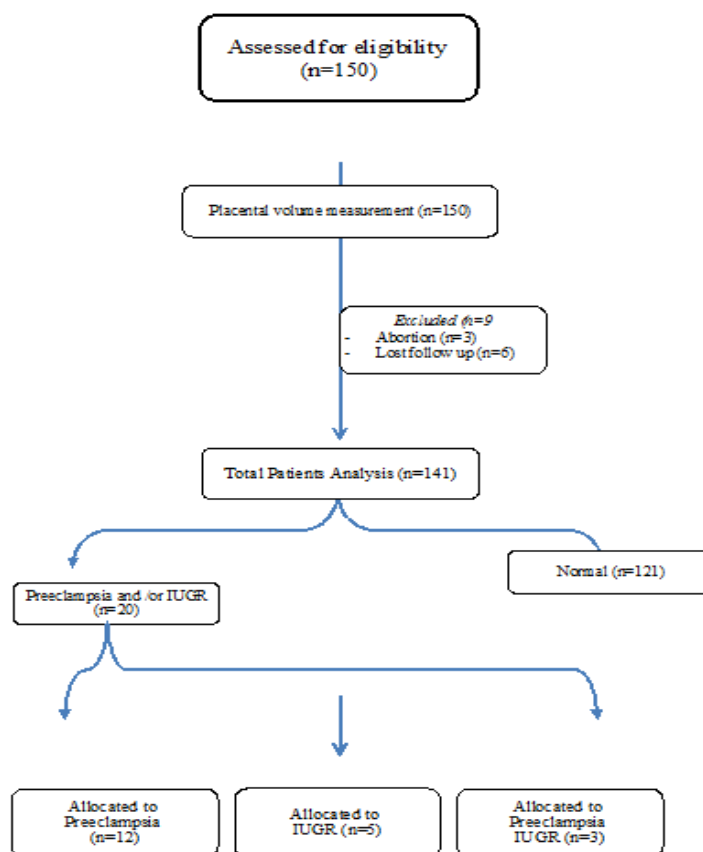

Fig.1: Flow chart of cases distribution.

Table 1 illustrates the basic characteristic data of the pregnant women in this study. There were no statistically marked differences in the BMI, parity, maternal ages and the mode of delivery between the pregnant women suffering from preeclampsia and women with normal   pregnancy.

	Total (n=141)
Age (years)	
Mean±SD	28.29±4.99
Range	18.82-41.08
BMI (kg/m^2)	
Mean±SD	27.66±3.74
Range	18.7-35.5
Parity	
P$_0$	48 (34.0%)
P$_1$	57 (40.4%)
P$_2$	30 (21.3%)
P$_3$	6 (4.3%)
Mode of delivery	
C.S	116 (82.3%)
VD	25 (17.7%)

Table 1: basic characteristic data of studied group.

Table 2: shows that the pregnant women with IUGR alone and preeclampsia alone and both   preeclampsia and IUGR had a significantly lower placental volume than the normal pregnancies (54.81 ± 9.03 , 48.78 ±8.13, 42.74 ±6.46 and 67.5 ± 8.45 cm3, p <.001). The pregnant women with IUGR and preeclampsia showed markedly lower placental volume.

This table showed that placental volume, V.I, F.I, V.F.I, and Uterine artery P.I. were significantly lower in IUGR with PET group and IUGR group versus normal group, (p-value<0.001).Further, placental volume and F.I were significantly lower IUGR and PET group compared to IUGR only group.

Variable	IUGR (n=5)	PET (n=12)	IUGR and PET (n=3)	Normal (n=121)	Test	p-value
Placental volume	54.81±9.03B	48.78±8.13C	42.74±6.46C	67.50±8.45A	27.849	<0.001**
V.I.	8.77±1.37B	8.35±1.24B	7.94±0.84B	10.06±1.57A	6.960	<0.001**
F.I.	49.40±2.67B	47.84±2.40C	46.28±2.80C	52.10±1.55A	35.538	<0.001**
V.F.I.	4.30±1.62B	3.95±1.46B	3.60±1.49B	5.44±0.76A	15.812	<0.001**
UAPI	2.06±0.25B	2.10±0.22B	2.13±0.14B	1.88±0.22A	5.509	<0.001**

Table 2: Comparing the studied groups according to first trimester uterine artery Doppler ,placental volume and placental vasculature.

Table 3 showed significant decrease in gestational age between both IUGR only and IUGR with PET group in comparison to normal group furthermore IUGR with PET group show significantly decreased gestational age in comparison to IUGR only group.

Variable	IUGR (n=5)	PET (n=12)	IUGR and PET (n=3)	Normal (n=121)	Test	p-value
Gestational age (day)	266.22±6.31B	257.79±5.68C	253.37±10.02C	276.32±4.25A	85.273	<0.001**
Birth weight (gm)	2652.2±137.3B	2408.8±123.6C	2325.4±318.4C	3456.8±178.9A	185.590	<0.001**

Table 3: Comparing the studied groups according to gestational age and birth weight.

Table   4.   Predictive   values   regarding   placental   volume   for   IUGR   and   preeclampsia   show parameters can markedly diagnose IUGR and PE with placental volume and flow index are most   accurete.

Variable	Sens.%	Spec%	PPV%	NPV%	AUC	95% C.I.	p-value
PV ≤54.6	68.5%	80.4%	52.1%	86.8%	0.799	0.73-0.86	<0.001**
V.I. ≤ 8.46	63.6%	74.6%	41.7%	85.1%	0.704	0.62-0.78	<0.001**
F.I. ≤ 49.4	78.3%	68.9%	40.2%	88.5%	0.771	0.70-0.85	<0.001**
VFI ≤ 3.66	48.9%	88.4%	66.4%	83.2%	0.682	0.58-0.78	<0.001**
P.I. ≥1.92	58.8%	62.0%	28.6%	82.3%	0.646	0.56-0.73	<0.001**

Table 4: Validity and predictivity of placental volume, V.I., F.I. and VFI and UAPI in prediction of   (IUGR & PE).

DISCUSSION

Complications of pregnancy related to the placenta causing IUGR have their pathophysiological basis in the first stages of placentation and can be obvious when the first trimester of pregnancy is ending near the completion of definitive placenta formation. Three vascular indices could illustrate the Intra-placental blood circulation: flow index (FI), vascularization index (VI), and vascularization flow index (VFI). Vascularization index is the relation between the number of color voxels and the whole number of voxels in the sampled tissue, so it detects the amount of vascularized tissue.[17]

In this study the placental volume was 64.58 ±11.34 cm3 which agreed with Guyomard et al which aimed to assess the distribution, reproducibility and feasibility of placental volume indices in relation to the crown-rump length within 11 weeks and 13 weeks 6 days where the mean ± SD of placental volume was 62.3± 14.8 cm3.[18]

In this study placental vasculature indices were V.I (mean ± SD) 9.78±1.7, F.I was (mean ± SD) 51.48±2.5, V.F.I was (mean ± SD) 5.19±1.19.

These results agree with González-González et al. results which aimed to assess placental volume, and perfusion parameter in association with biochemical markers PAPP-A for screening of IUGR.The results of his study showed V.I was 9.49±4.57 , F.I 48.8±4.56 and V.F.I 4.73±2.53. These results disagree with Nia Wyn Jones et al. (2011) results in which V.I was 13.24± 7.06, F.I 46.62± 4.08 and V.F.I was 6.38± 3.76 which showed significantly higher placental vascular indices.[19]

This also disagrees with Mohamed et al. study which studied placental vasculature in healthy non diabetic pregnancies and pregnancies with pregestational diabetis , the placental vasculature indices were V.I 12.1 ±2.62 , F.I was 34.5 ± 9.6 and V.F.I was 6.5+ 1.1 which also showed significantly higher placental vasculature indices than our study group who had previous IUGR.[20]

Uterine artery pulsatility index was 1.92±0.25. This agrees with Augusto et al. which assessed uterine artery pulsatility index reference ranges parameter between 11 wk : 14 wk and the mean value was 1.5 + 0.5.[21]

In this study, 5 patients had IUGR alone and 12 had PET alone and 3 patient had IUGR with PET. This disagrees with González-González et al. who showed increased incidence of PET with IUGR but with incidence 30 case of IUGR with PET out of 193 case of IUGR (15.5%).[19]

Soongsatitanon et al. also studied 1st trimester placental volume and vasculature in prediction of IUGR and PET. They measured the placental volume during the first-trimester aneuploidy screening using transabdominal 3D ultrasound. We measured the predictive values of this examination. Data was gathered from 360 pregnant women then it was analyzed, we found that IUGR and/or preeclampsia were established in seventeen cases. The cut-off level was determined according to the 10th percentile of placental volume. The specificity, sensitivity, positive and negative predictive values of placental volume for prediction of IUGR and/or preeclampsia were found to be 90.7%, 23.5%, 11.1% and 96%, respectively. The specificity, sensitivity, positive and negative predictive values for prediction of early onset preeclampsia were found to be 90.7%, 50%, 3.0% and 99.7%, respectively. [22]

This agree with our study regarding the specificity and negative predictive values but our results show higher sensitivity and positive predictive values than the results of Soongsatitanon et al. study.[22]

In this study we found that decrease in placental volume and vascularity was associated also with increased incidence of PET with IUGR which can be attributed to the same pathogenesis of defective deep placentation which occurs in both IUGR and preeclampsia.

CONCLUSION

our study demonstrated that the quantitative assessment of first trimester placental vasculature and placental volume in association with uterine artery Doppler can be considered a promising modality for early prediction of IUGR and/or PET.

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