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Value of 3D Ultrasonographic Assessment of Placental Volume and Perfusion Indices in The First Trimester as a Predictor to the Occurrence of Preeclampsia

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ABSTRACT

Background: Preeclampsia (PE) is one of the hypertension illnesses associated with pregnancy, affecting 3-5% of pregnant women, and is a significant cause of maternal morbidity and perinatal mortality. Detection of placenta changes in the first trimester by three-dimensional power-Doppler ultrasound can be used to detect preeclampsia early.

Objective: The aim of the current work was to demonstrate if 3D- Indicators of placental volume and vascular flow in the first trimester might predict preeclampsia.

Patients and methods: This prospective cohort study included 324 pregnant women with singleton pregnancies, attending at Prenatal Care Outpatient Clinic, Zagazig University Hospitals for regular antenatal care between weeks 11 + 0 and 13 + 6 of pregnancy. Transabdominal the 3D power Doppler ("placental biopsy") was used to assess placental vascularization. Making use of the Virtual Organ Computer-aided Analysis (VOCALTM) imaging tool, the obtained spherical volume was analyzed. three vascular indices, were calculated: Index of vascularization (VI), vascularization- flow index, as well as flow index (VFI).

Results: A comparison of placental volume of healthy pregnancy group and preeclamptic pregnancies in the current study showed a statistically significant considerable distinction (P value 0.001). The mean volume in the two groups was 84.9±22.3 and 45.6±11.4 cm^3, respectively. The volume of the placenta was higher in the healthy pregnancy group compared to preeclamptic pregnancy group. In addition, a comparison between normal pregnancy and pregnancies with PE, in terms of FI, VI, and VFI, indicated a difference that is statistically significant (P value 0.001). The averages of FI, VI, and VFI in the two groups were (95.4±9.1, 24.7±8.1, 13.1±3. 7) and (16.2±5.8, 54.6±10.9, 8.1±2.1) respectively. These findings clearly reveal that placentas from preeclampsia complicated pregnancies have lesser blood vessels (reduced VI) and lower blood flow (reduced FI). According to our findings, this ultrasonographic technology can forecast the development of PE.

Conclusions: It could be concluded that the quantitative measurement of placental vasculature and volume using noninvasive 3D Power Doppler and the VOCAL™ technique during the first trimester may be utilized to predict preeclampsia. Patients who later develop preeclampsia tend to have decreased placental volume and poorer 3DPD indices in this critical area during the first trimester.

Keywords: preeclampsia, tree-dimensional ultrasound, screening, vascular indices, Doppler.

INTRODUCTION

Preeclampsia constitutes the commonest medical disorder diagnosed by obstetricians in clinical practice representing 7% to 9% of every pregnancy. It is the main factor in maternal and perinatal mortality around the world [(1)].

The placenta, which serves as a fundamental connection between the fetus and the mother for endocrine function, metabolic exchange as well as additional physiological processes, is crucial for maternal neonatal health.

As a result, evaluation of the placenta with ultrasonography throughout pregnancy is a crucial component of pregnancy care.

In the later stages of pregnancy, placental ultrasonography is primarily used to determine the position of the placenta and diagnose anomalies. However, the development of high-resolution transvaginal ultrasonography has changed how we perceive placental development research, also believed to be early pregnancy placental examination might be valuable in recognizing the risks for later diseases **[(2)].**

Normal intervillous space formation within healthy fetal-maternal relations depend on the first trimester connection. Small-caliber spiral arteries are transformed by trophoblasts into large uteroplacental vessels that carry blood to the intervillous space and, eventually, the placenta is compressed is important to this inadequate spiral artery remodeling, leading in reduced blood supply has been connected to the pathophysiology of preeclampsia **[(3)].**

The start of preeclampsia may not be anticipated only by risk factors and maternal history, particularly in nullipara women. Prenatal care focuses mostly on assessing the fetus's development and is the cause of many antenatal hospitalizations. As a result, much study has been devoted to improving the prediction of preeclampsia **[(4)].**

Advances in ultrasound technology and understanding of the pathophysiology of preeclampsia have rekindled efforts to establish a screening approach for the illness, with the emphasis shifting to identifying a

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monitoring program for first trimester. Several initiatives have previously been made to distinguish high-risk and first-trimester low-risk pregnancies. In the first trimester, for example, 90 mmHg for the mean arterial blood pressure or above related to a higher risk of preeclampsia [(5)].

First trimester uterine artery doppler alone has only shown modest detection performance for preeclampsia. This might be since these approaches provide an indirect evaluation of the aberrant placentation process [(6)].

Free vascular endothelial growth factor (VEGF), soluble fms-like tyrosine kinase-1 (sFlt-1), PAPP-A, inhibin A, PP 13, Activin A, and serum tumor necrosis factor-alpha receptor-1 (TNF-R1), and soluble endoglin have all been shown poor to moderate predictors of preeclampsia [(7)].

An intriguing element might be a direct evaluation of trophoblastic invasion, which is linked to the development of preeclampsia. With the advent of 3-dimensional (3D) ultrasound technology that allow for the imaging of vascular volumes, early alterations in the uteroplacental circulatory space (UPCS), which is made up of maternal vasculature and the space between them, may now be measured [(8)].

The aim of the current work was to demonstrate the role of first-trimester three-dimensional (3D) power Doppler of placental blood flow and 3D placental volume in early prediction of pre-eclampsia and to assess the efficacy of various ultrasonographic parameters such as uterine artery doppler, placental thickness, and placental placement when making preeclampsia predictions. This is to improve quality of the health of mother, fetus, and infant.

PATIENTS AND METHODS

This prospective cohort study included 324 pregnant women with singleton pregnancies, attending at Prenatal Care Outpatient Clinic, Zagazig University Hospitals for regular antenatal care between weeks 11 + 0 and 13 + 6 of pregnancy. This study was conducted between June 2016 and June 2017.

Inclusion criteria: Women with a singleton pregnancy who were evaluated between 11 and 13 + 6 weeks with a verified viable intrauterine pregnancy, no current bleeding, and no indications of subchorionic hematoma. Unless there was a difference from the first-trimester ultrasound that exceeded 5 days, the beginning of the last regular menstrual cycle was used to establish the gestational age.

Exclusion criteria: Multifetal pregnancy, fetal malformations, and hampered volume measurement by uterine malformations or fibroids.

All women were subjected to:

Direct questioning and study of medical notes were used to acquire demographic data from each lady. This included:

1) Personal information: name, age, address, profession, and any peculiar behaviors.
2) Obstetric history: Gravidity, parity, number of abortions, previous pregnancies with preeclampsia.
3) Menstrual history: Last Menstrual Period (LMP), Menarche, regularity of cycle, and Expected Date of Delivery (EDD).
4) Chronic hypertension, antiphospholipid syndrome, diabetes, sickle cell disease, thrombophilia, and other common medical comorbidities are all part of the patient's medical history.
5) Medication (which may include antidepressant, antihypertensive, antithyroid, antiepileptic, β-mimetic, aspirin, steroids, insulin, and thyroxin).

Complete general examination:

Vital Signs (Body Temperature, Pulse Rate, Respiration Rate & blood pressure), maternal weight and height, body Mass Index, chest and heart examination and lower limb examination: for edema

The patient's blood pressure was taken while seated, with the cuff of a mercury sphygmomanometer placed on the patient's right arm at the level of heart. The Korotkoff IV sound (The point at which the sound becomes muffled) was used for the diastolic blood pressure.

Obstetric examination during follow-up visits: Fundal grip, fundal level, pelvic grips and umbilical grip.

Laboratory investigations: Urine analysis, random blood sugar, blood grouping, Rh typing, complete blood count (CBC), Liver function tests (protein – albumin– bilirubin – ALT-AST) and kidney function tests (urea and creatinine).

Ultrasound data acquisition:

Voluson 730 pro V (General Electric Medical Systems, Austria) ultrasonography was used, along with a volumetric multi-frequency abdominal probe (2.2-6.5 MHZ).

The following procedures were applied for each case:

- According to **Hasija *et al.*** [(9)], 2D ultrasound scanning is used to evaluate fetal biometric data, fetal morphology, and placental localization. The uterine arteries and pulsatility were identified and resistance indexes were calculated bilaterally.
- The use of the VOCAL technique and 3D power Doppler to measure placental volume (PV) and placental vascular indices; vascularization-flow index (VFI), flow index (FI), and vascularization index (VI).
- Ultrasound examinations were performed by one observer only.

Assessment of uterine artery Doppler:

The uterus' sagittal slice was examined taken for Doppler studies of the uterine artery, When the internal cervical os and cervical canal were discovered. After that, the transducers were gently moved from edge to edge, and colored flow imaging was used to locate each uterine artery. Pulsed wave Doppler imaging with a sampling gate of 2 mm and an insonation angle of less than 30 degrees was used to examine the whole blood artery (Fig. 1). After producing three similar subsequent waveforms, on both sides, the PI and RI were measured, and the average values of the left and right arteries were computed [(10)].

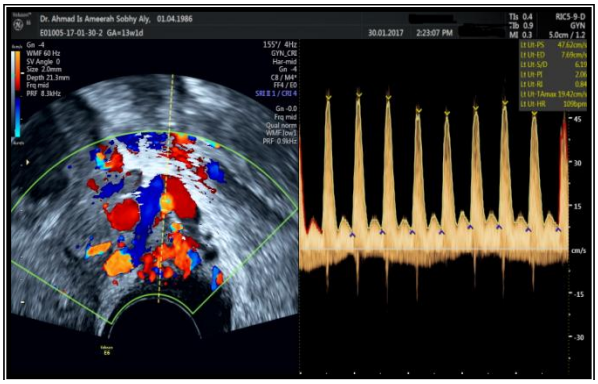

Fig. (1): Acquisition of utrine artery doppler

Assessment of placental volume:

Transabdominal sonography was used to get a 3D volume of the placenta. The probe was positioned with the sweep angle set at 85 degrees. parallel a placental plate. The placenta was checked, and the volumetric box's dimensions were altered so that the placenta fit entirely inside. The volume was then saved for offline analysis later.

Virtual Organ Computer-aided Analysis (VOCAL™) approach was then utilized to obtain a succession of placental sections, each taken 30 rotations from the preceding one for a total of 180˚. The outline of the placenta was hand sketched in each of the six planes, taking care to eliminate the uterine wall. The uterine wall is frequently thicker under the placenta during this stage of pregnancy, either owing to hypertrophy or contraction. Each volume was measured twice: first when the computer made a volume calculation using the highlighted locations in each of the six planes, followed by the calculation was complete. The volume was presented alongside the calculated reconstruction of the organ (Fig. 2).

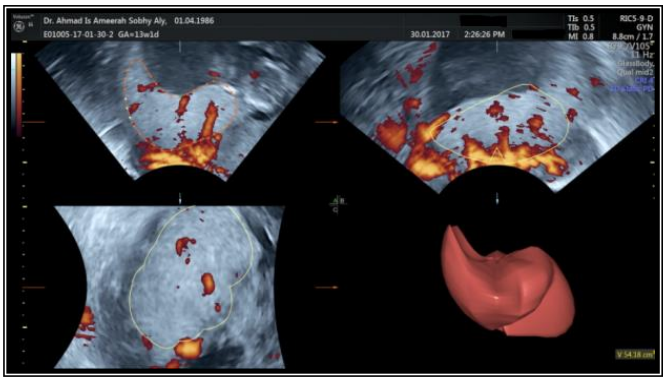

Fig. (2): acquisition of placental volume

Evaluation of placental vascular indices:

A 3D power Doppler technique was used to analyze blood flow in the placenta. The entire placenta was positioned inside the region of interest and subjected to a power Doppler scan. After accepting the VOCAL at 30 and applying a region of interest, which automatically computes FI, VI, and VFI values for the total placental volume, A volume histogram is produced after recording the power Doppler in 3D.

VI (0 to 100) represents the proportion of placental volume exhibiting a flow signal. FI represents the average flowing signal intensity within the placenta (0-100). Multiplying VI and FI yields VFI (0-100), a combination of vessel presence data and flowing level.

Follow up:

All cases were followed up regularly until delivery (once monthly for the first six months of pregnancy, twice monthly during the seventh and eighth month and then once weekly till delivery).

In Follow up visits:

- Blood pressure was measured using mercurial sphygmomanometers that have been regularly and previously calibrated intervals throughout the trial.
- Each visit, a mid-stream urine sample was obtained to identify albuminuria using dipsticks, and a 24-hour urine collection was evaluated for proteinuria if dipstick analysis of midstream urine specimens is one plus or more.
- Examine the lower limb for edema and its level if present by pushing the thumb on the tibia in the case of leg edema and pinching in the case of greater edema.
- Maternal weight gain was assessed in each visit to exclude internal edema.
- Abdominal ultrasonography to determine embryonic viability, estimate biometry, and detect growth limitation.

Outcome measures:

- The key outcome data were whether or not the patients developed preeclampsia.

- The type of delivery whether vaginal delivery or Caesarian section for each patient, for each instance, the birth weight, gestational age at delivery, and neonatal outcome were documented.

The American College of Obstetrics and Gynecology developed a criteria for preeclampsia.

Patients presenting with 0.3g or more of protein is considered to be proteinuria after 20 weeks of pregnancy. excretion in a 24-hour urine sample. Systolic blood pressure needs to be at least 140 mm Hg, and diastolic pressure ought to be at least 90 mm Hg. [(11)].

A lady with blood pressure that was previously normal and 300 mg of protein in a 24-hour urine test sample or +1 on the urinalysis was diagnosed with mild preeclampsia at 20 weeks pregnant.

Acute preeclampsia has been diagnosed in patients with preeclampsia using one of the following criteria: Proteinuria of at least 5 g or +3 on urinalysis in two separate samples taken at least 4 hours apart, vision impairment or other neurological problems, oliguria (500 ml of urine in 24 hours), chronic epigastric discomfort, hypoamniotic fluid Headache, increased liver enzymes, and fetal development limitation are all symptoms [(12)].

Alexander *et al*. [(13)] used a growth chart to define tiny foetal weight in the 10th percentile for gestational age as measured by weight during gestation.

Ethical consideration:

This study was ethically approved by Zagazig University's Research Ethics Committee. Written informed consent of all the participants was obtained, along with a description of management approach and a follow-up plan. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

The data was statistically characterized based on the mean and standard deviation (SD). The chi-Square Categorical data were compared using the (X2) test. The ideal cut-off value for the examined diagnostic indices was established using ROC analysis, or receiver operator characteristic, analysis. P value of less than 0.05 was required for statistical significance. For all statistical analyses, SPSS software was utilized.

RESULTS

A total of 340 participants were included in the study. Seven patients (2.1%) had spontaneous abortions in the second trimester before 24 weeks of pregnancy, and nine patients (2.6%) lost in the follow-up. Of the remaining 324 individuals, 44 (13.6%) established preeclampsia, whereas 280 (86.4%) did not. 18 (40.9%) of individuals with preeclampsia were diagnosed with severe preeclampsia. 17 (38.6 percent) experienced preeclampsia, necessitating delivery before 34 weeks. 4 preeclamptic patients (9.1 percent) gave birth to a child that was small for gestational age (SGA), with birth weights below the 10th percentile, whereas 14 patients (5.0 percent) gave birth to an SGA infant without preeclampsia.

The data of the remaining cases (324) were classified into two groups:

- Unaffected (normal) group: cases that did not develop preeclampsia (n = 280 cases = 86.4%).
- Affected group: Overall preeclampsia group = all cases that developed preeclampsia (n = 44 cases = 13.6%).

Table 1 shows that the mean age was **27.4±9.1 years**, body mass index (BMI) was **31.9±10.7 kg/m^2** and the crown rump length at time of enrollment ranged from 43.7 to 84.

Table (1): The uterine artery Doppler at the 1st trimester among studied groups.

Uterine artery	Unaffected	Affected	T	P
PI - mean±SD *Range	0.76±0.14 0.6-0.9	1.14±0.37 0.9-1.5	11.9	<0.001
RI - mean±SD *Range	0.49±0.1 0.42-0.55	0.58±0.1 3 0.52-0.72	4.9	<0.001

Uterine artery Doppler PI and RI were suggestively higher in preeclampsia (Table 1).

Three D power Doppler indices of placenta were significantly lower in preeclamptic cases (Table 2).

Table (2): 3D power Doppler indices of placenta at the 1st trimester among the studied groups

	unaffected	affected	T	P
VI	24.7±8.1	16.2±5.8	9.7	<0.001
FI	95.4±9.1	54.6±10.9	6.1	<0.001
VFL	13.1±3.7	8.1±2.1	12.9	<0.001

The placental volume was significantly lower in preeclampsia cases than control (Table 3).

Table (3): Placental volume evaluation by 3D-ultrasound.

Placental volume (cm^3)	unaffected	affected	T	P
Mean±SD Range	**84.9±22.3 54.2-152.9**	**45.6±11.4 33.5-62.4**	**11.9**	**<0.001**

VFI had better sensitivity, specificity, and accuracy than FI and VI (Table 4).

Table (4): The diagnostic value of the uterine artery Doppler and placental volume in the prediction of PE.

	VI	FI	VFI
CUT OFF	**<22.7**	**<51.3**	**<10.4**
SENAITIVITY	**81.3**	**86.4**	**88.6**
SPECIFICITY	**71.4**	**70.7**	**75.8**
PPV	**31.3**	**34.8**	**39.1**
NPV	**94.7**	**88.4**	**80.4**
ACCURACY	**72.2**	**68.7**	**78.1**

DISCUSSION

Many first-trimester prediction methods for PE have been created, but there is currently no viable a single screening procedure to detect high-risk females prior to the symptoms suggestive of PE. The use of these prediction models may enhance risk selection by allowing for early detection and the implementation of preventative actions [(14)].

With the advent of 3D ultrasound technology that allow for the imaging of vascular volumes, it is now possible to investigate early alterations in the uteroplacental circulatory space (UPCS). The placenta's vascular indicators are computed using data in three dimensions created by voxels (the fundamental information units of volume) for organ and structural vascularization evaluation. The overall and proportional quantities in the amount of interest of power Doppler information are represented by these indices [(15)].

Efficacy of uterine artery Doppler study the accuracy of pre-eclampsia prediction widely studied, first in the middle of the pregnancy's second trimester and, more lately, its early stages. Pre-eclampsia is characterized by aberrant placentation, which is correlated with greater resistance in the uteroplacental circulation. The presence of a diastolic notch in the uterine artery's an increase in the pulsatility index or a Doppler waveform (PI) of that vessel are ultrasonographic indicators of this resistance. Several trials had different variations in test results for vascular impedance, gestational age at preeclampsia prevalence, screening, and preeclampsia diagnosis [(15)].

In terms of mean uterine artery PI, the current study stated that preeclamptic patients had considerably greater UADPI than controls. This was in line with the conclusions of **Plasencia *et al.*** [(16)], who reported that Doppler examinations Studying the uterine arteries between 11 and 13 weeks revealed that flow impedance is raised in pregnancies where hypertension subsequently develops illnesses, additionally, the growth is especially pronounced in early PE.

Parra-Cordero *et al.* [(17)] sought to construct a prediction model to treat preeclampsia during the first trimester of pregnancy by biochemical, incorporating clinical, and ultrasound indications. In a pre-eclampsia screening experiment, 5367 asymptomatic between 11+0 and 13+6 weeks gestation, pregnant women were evaluated. They discovered that the control group's lowest UADPI, expressed as MoM, was considerably lower than both the early and late onset preeclamptic groups. The detection rate according to that result of combined history taking and uterine artery PI was 43.8% and 28.3% when comparing early and late PE.

Additionally, **Velauthar *et al.*** [(18)] conducted a meta-analysis of the uterine artery Doppler's ability to predict outcome studies for preeclampsia beginning in the first trimester. Reviewing 18 trials including a total of 55 974 women, in fifteen of these investigations, women with low-risk pregnancies were enrolled. The aberrant flow velocity waveforms were defined using the 90th percentile of the uterine artery RI or PI. With sensitivities of 26.4% and 47.8%, respectively, in the first trimester, an abnormal uterine artery PI indicated preeclampsia and early-onset preeclampsia.

In contrast to our findings, **Napolitano *et al.*** [(19)] found no statistically significant difference in the screening sensitivity for preeclampsia prediction between low, medium, and high indices of uterine artery resistance.

In research on the first-trimester uterine artery Doppler analysis's predictive power, **Khong *et al.*** [(20)] determined that the predictive accuracy of first-trimester uterine artery Doppler is superior for identifying early onset. In addition, they have claimed that preeclampsia and FGR are diseases with a late beginning. Sensitivity and particularity of the uterine artery in low-risk populations, the Doppler indices for predicting preeclampsia vary from 34 to 76 percent and 83 to 93 percent, respectively. They reported that the limited sensitivity of this test restricts its value as an isolated disease marker.

The reasons for the limited sensitivity and anticipated accuracy of first trimester uterine artery Doppler testing when employed as a screening tool in low-risk individuals, uterine artery impedance may be influenced by a variety of factors, such as maternal length, uterine size, gravidity, placental volume, trophoblast activity, etc. As a result, variations in uterine artery impedance are not induced by spiral arterial remodeling. They are, however, dependent on other parameters, which can result in varied development, adaption, and velocity until the eventual endpoint of low impedance and no notching is reached. After around 24 weeks, solid evidence may be collected, and judgments can be drawn [(20)].

The emergence of 3D ultrasonography has enabled the measurement measure placental volume. In vitro experiments suggest that the VOCAL approach may be more accurate in estimating the volume of an irregular item, such as the placenta [(21)].

In numerous research, sonographic evaluation of placental volumes has been recommended as a method for predicting intrauterine growth restriction or pre-eclampsia. In the present research, a comparison of normal and abnormal placental volumes pregnancy and preeclamptic pregnancies revealed a statistically significant difference (P value <0.001). The mean volume in the two groups was 84.9+_22.3 and 45.6+_11.4 cm^3, respectively. The volume of higher in the placenta in the healthy pregnancy group than in the preeclamptic pregnancy group.

The same outcomes were reported by **Hashish *et al.*** [22], who discovered a statistically significant variation in placental volume between these pregnancies that developed PE compared to unaffected gestations (49.7 ± 31.6 vs. 91.8 ± 32.6, p<0.001). They postulated that inefficient placentation, as shown by a decrease in placental volume between 11 and 13 weeks contributes to the eventual development of PE during pregnancy.

In contrast to our findings, **Odibo *et al.*** [23] found that the average placental volumes in the first trimester of these fetuses with PE were not considerably different from those of unaffected pregnancies. When the mean placenta volume was lower in GH and SGA pregnancies than in normal controls, this result was in contrast. GH and SGA prediction models based on placental volume were less accurate than PE prediction models based on vascular markers.

In a comparable investigation, **Chen *et al.*** [24] demonstrated no significant change in placental volumes between the SGA and control groups.

Differences in machine settings, placental volume acquisition methods and study sample sizes might all contribute to the disparities in results.

In another investigation performed by **Pimenta *et al.*** [25] to evaluate the placenta, 3D power Doppler sonography was employed volumes and vascularity in normal pregnancies and pregnancies complicated by hypertensive disorders. These The placental volumes of the groups did not differ statistically, and their findings do not support the idea that pregnancies are made more difficult by hypertension illnesses corresponding to smaller placentas.

It was considered that the 3D perfusion indices, such as the FI, VI, and VFI, may reflect blood flow in the utero- and feto-placenta when used to quantify placental perfusion [15].

A comparison of placental FI, VI, and VFI between normal pregnancy and pregnancies that had PE indicated a statistically significant difference in the current research (P value <0.001). The mean FI, VI, and VFI values in the two groups were (95.4±9.1, 24.7±8.1, 13.1±3.7) and (54.6±10.9, 16.2±5.8, 8.1±2.1) respectively. These results demonstrate conclusively that placentas from preeclampsia-affected Pregnancy is associated with decreased blood flow (reduced FI) and fewer blood vessels (reduced VI). According to our findings, this ultrasonographic technology has the ability to forecast the progression of PE.

Dar *et al.* [3] stated that 3D first trimester power Doppler (3DPD) of the UPCS varied between preeclamptic and non-preeclamptic women. 3DPD indices throughout the first trimester of the UPCS were lower in PE patients, according to the researchers. In addition, they anticipated that testing for FI, VI, and VFI in early pregnancy might be a useful method of first-trimester pregnancy screening -related condition.

Dar *et al.* [3] also stated that 3DPD investigations of placental vascular indices at 10-14 weeks were lower in women with PE, corroborating our results.

In their study, **Odibo *et al.*** [23] found the first-trimester placentas' mean vascular indices were lower fetuses that eventually compared to pregnancies without the condition, developed PE in their research. Furthermore, both PE and SGA pregnancies had considerably reduced FI as in contrast to controls. The PE prediction models based on these indices, however, were linked with very limited discriminating capacity, as evidenced by AUC values of around 70%. Poor detection rates for PE with FI, VI, and VFI, with significant false positive rates, despite statistically significant increases in mean values.

Contrary to our findings, **Hannaford *et al***. [26] found no statistically significant alterations in placental vascular parameters in women with PE. Although the authors indicate lower average value for FI, VI, and VFI in pregnant women who have PE as well as those with early PE, these results are not statistically meaningful. Considering the small quantity of PE cases in the research, this may be seen as a lack of power.

Hannaford *et al*. [26] and **Hashish *et al.*** [22] presented enough data on PVI sensitivity and specificity. In the **Hannaford** study, VI and VFI most accurately predicted early-onset PE; however, **Hashish *et al.*** report a sensitivity of 80% and a specificity of 92.1% for VFI in high-risk women.

CONCLUSION

It could be concluded that the quantitative measurement of placental vasculature and volume using 3D Power Doppler and the VOCAL™ technique during the first trimester may be utilized to predict preeclampsia.

Preeclampsia-complicated placentas have a smaller volume, decreased blood flow (reduced FI), and fewer blood vessels (lower VI).

More research is needed to understand if this reduced vascularization contributes to hypertension problems in pregnancy.

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REFERENCES

1. **Scott G, Gillon E, Pels A *et al.* (2022):** Guidelines Similarities and dissimilarities: A systematic review of international clinical practice guidelines for pregnancy hypertension. American Journal of Obstetrics and Gynecology, 226(2): 1222-1236.
2. **Bowman E, Arany Z, Wolfgang J (2021):** Regulation of maternal–fetal metabolic communication. Cellular and molecular life sciences, 78(4): 1455-1486.
3. **Dar P, Gebb J, Reimers L *et al*. (2010):** First-trimester 3-dimensional power Doppler of the uteroplacental circulation space: a potential screening method for preeclampsia. Am J Obstet Gyneco.l, 203(238): 1-7.
4. **Poon C, Kametas A, Chelemen T *et al.* (2010):** Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. J Hum Hypertens., 4:104-110.
5. **Cnossen S, Vollebregt C, de Vrieze N *et al.* (2008):** Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: systematic review and meta-analysis. BMJ., 336(7653):1117-1120.
6. **Phan K (2019):** Evaluation of Arterial Stiffness, Wave Reflection, and Hemodynamics Preceding Pre-eclampsia Onset in High-Risk Pregnant Women. McGill University (Canada). https://www.proquest.com/openview/42d2ef22ebd2e1688eac6b909cf62234/ 1?pq-origsite=gscholar&cbl=18750&diss=y
7. **Akolekar R, Cuz J, Foidart M *et al*. (2010):** Maternal plasma soluble fms-like tyrosine kinase-1 and free vascular endothelial growth factor at 11 to 13 weeks of gestation in preeclampsia. Prenat Diag., 116:268.
8. **Khalil A, Cowans J, Spencer K *et al.* (2009):** First trimester maternal serum placental protein 13 for the prediction of pre-eclampsia in women with a priori high risk. Prenat Diagn., 29:781-789.
9. **Hasija A, Balyan K, Debnath E *et al.* (2021):** Prediction of hypertension in pregnancy in high risk women using maternal factors and serial placental profile in second and third trimester. Placenta, 104: 236-242.
10. **Prefumo F, Canini S, Casagrande V *et al.* (2006):** Correlation between first-trimester uterine artery Doppler indices and maternal serum free beta-human chorionic gonadotropin and pregnancy-associated plasma protein A. Fertil Steril., 86(4):977-980.
11. **American College of Obstetricians and Gynecologists (2013):** Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in pregnancy. Obstet Gynecol., 122:1122-1134.
12. **American College of Obstetricians and Gynecologists (2012):** Diagnosis and management of preeclampsia and eclampsia. Practice Bulletin No. 33. https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0033-1349895
13. **Alexander R, Himes H, Kaufman B *et al*. (1996):** United States national reference for fetal growth. Obstet Gynecol., 87:163-171.
14. **Kleinrouweler E, Cheong-See M, Collins S *et al*. (2016):** Prognostic models in obstetrics: available, but far from applicable. American journal of obstetrics and gynecology, 214(1):79–90.
15. **Antonio-Guimarães H, da Costa L and Júnior A (2008):** Angiogenesis and vascular assessment through three-dimensional power Doppler ultrasonography. Arch Gynecol Obstet., 277:195-200.
16. **Plasencia W, Maiz N, Bonio S *et al*. (2007):** Uterine artery Doppler at $11^{+}0$ to $13^{+}6$ weeks in the prediction of preeclampsia. Ultrasound Obstet Gynecol., 30:742-749.
17. **Parra-Cordero M, Rodrigo R, Barja P *et al.* (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): 538-544.
18. **Velauthar L, Plana N, Kalidindi M *et al.* (2014):** First-trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55,974 women. Ultrasound Obstet Gynecol., 43(5):500-507.
19. **Napolitano R, Rajakulasingam R, Memmo A *et al.* (2011):** Uterine artery Doppler screening for pre-eclampsia: comparison of the lower, mean and higher first-trimester pulsatility indices. Ultrasound Obstet Gynecol., 37(5):534-537.
20. **Khong L, Kane C, Brennecke P *et al.* (2015):** First-Trimester Uterine Artery Doppler Analysis in the Prediction of Later Pregnancy Complications. https://www.hindawi.com/journals/dm/2015/679730/
21. **Sakata T & Vehrencamp L (2012):** Integrating perspectives on VOCAL performance and consistency. The Journal of Experimental Biology, 215(2):201-209.
22. **Hashish N, Hassan A, El-Semary A *et al.* (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):1094-1098.
23. **Odibo O, Goetzinger R, Huster M *et al*. (2011):** Placental volume and vascular flow assessed by 3D power Doppler and Adverse pregnancy outcomes. Placenta, 32(3):230-234.
24. **Chen J, Chen P, Sun J *et al*. (2019).** Comparison of placental three-dimensional power Doppler vascular indices and placental volume in pregnancies with small for gestational age neonates. Journal of clinical medicine, 8(10): 1651-1659.
25. **Pimenta A, de Paula S, Campos B *et al.* (2014):** Three-Dimensional Sonographic Assessment of Placental Volume and Vascularization in Pregnancies Complicated by Hypertensive Disorders J Ultrasound Med., 33:483-491.
26. **Hannaford E, Tuuli M, Goetzinger R *et al.* (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):965-970.