



ROLE OF SHEAR WAVE ELASTOGRAPHY OF PLACENTA IN NORMAL AND PRE-ECLAMPTIC PREGNANCIES IN THIRD TRIMESTER

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ABSTRACT

Pre-eclampsia (PE) is a pregnancy-related condition characterized by new-onset hypertension (with systolic blood pressure > 140 mm Hg and diastolic blood pressure > 90 mm Hg on two occasions at least 4 hours apart, or more severe cases with higher values) along with proteinuria (elevated protein levels in urine). This condition resolves within the first 6 weeks after childbirth. This abnormal placental attachment and ineffective invasion of trophoblast cells into the muscular spiral arteries leads to hypoxia and placental ischemia. Shear wave elastography (SWE) is an innovative ultrasound technique designed to assess the elasticity of soft tissues. In the placenta, increased stiffness is a consequence of ischemia-related processes including inflammation, necrosis, infarction and fibrosis. The present study is planned to assess the utility of SWE in evaluation of placental function and can be used as a supplement to existing methods for prediction of PE.

KEYWORDS : Pre-Eclampsia, Shear Wave Elastography, Placenta, Elasticity, Placental Stiffness, pascal(kPa).

INTRODUCTION

Pre-eclampsia (PE) is a disorder of pregnancy characterized by onset of hypertension and proteinuria after 20 weeks of gestation. PE significantly contributes to perinatal and maternal mortality and impacts approximately 5% to 7% of pregnant women globally.^{1,2}

PE is a pregnancy-related condition characterized by new-onset hypertension (with systolic blood pressure (SBP) > 140 mm Hg and diastolic blood pressure (DBP) > 90 mm Hg on two occasions at least 4 hours apart, or more severe cases with higher values) along with proteinuria (elevated protein levels in urine). This condition typically occurs after 20 weeks of gestational age and resolves within the first 6 weeks after childbirth.³ PE is divided into two distinct types: Early-onset, which occurs before 34 weeks of gestation and Late-onset, which manifests at or after 34 weeks of gestation.

PE is primarily attributed to inadequate placental implantation in the uterine lining. This abnormal placental attachment results in impaired utero-placental blood flow, inflammation & endothelial dysfunction. Ultimately, ineffective invasion of trophoblast cells into the muscular spiral arteries prevents the transformation of arteries into "low-resistance" capacity vessels. This leads to hypoxia and placental ischemia reducing the supply of nutrients to the fetus.^{4,5}

Early identification and effective management of PE are crucial for enhancing the well-being of mother and fetus.⁶ The accuracy of PE screening has been improved by combining maternal blood biochemical markers with maternal biophysical indicators, such as uterine artery Doppler and mean arterial pressure.⁷

Sonoelastography is a method that can detect variations in the elasticity or stiffness of tissues. Elasticity, in this context, pertains to the way materials respond when subjected to reversible deformation. Changes in the soft tissue stiffness can occur due to a range of physiological or pathological factors. Shear wave elastography (SWE) is an innovative ultrasound technique to assess the elasticity of soft tissues. It operates by generating mechanical vibrations through acoustic radiation force, capturing the lateral propagation of transverse shear waves emanating from the tissue and measuring their velocity.^{8,9}

SWE is a viable technique for assessing the elasticity of placenta.¹⁰ In the placenta, increased stiffness is a consequence of ischemia-related processes including inflammation, necrosis, infarction and fibrosis.^{11,12} As an addition to current techniques for PE prediction, the present study aims to evaluate the usefulness of SWE in placental function assessment.

OBJECTIVES

- To assess placental stiffness by shear wave elastography in third trimester.
- To compare placental elastography findings in normal and pre-eclamptic pregnancies in third trimester.

MATERIALS AND METHODS

Source of Data

This is a hospital-based, prospective case control study conducted in the department of Radio- Diagnosis, at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar, over a period of 18 months from September 2022 to February 2024.

Methodology

A total of 134 patients were included: 67 patients in pre-eclampsia group and 67 subjects in normal pregnant women group referred for obstetric scan to the department of Radio-Diagnosis at the R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar. The study was conducted following approval from the institutional ethical committee. A written consent form was obtained from all patients fulfilling the inclusion criteria after explaining the objective, procedure, and expected outcome in detail before the start of the study. The patients were included in the study based on the inclusion and exclusion criteria

Inclusion Criteria:

- All normal pregnant women
- All pre-eclampsia patients in third trimester referred to Department of Radio-diagnosis for obstetric scan

EXCLUSION CRITERIA

- Placental anomalies
- Posterior placental location
- Gross calcification of placenta
- Twin pregnancy
- Pre-existing medical conditions like chronic hypertension, chronic renal disease, uncontrolled diabetes mellitus, systemic lupus erythematosus (SLE), maternal infections.

Method

Shear wave elastography is performed by using shear wave technique. The placental image will centre in the field of view. The fixed-size region of interest (ROI), a rectangle measuring 1×0.5 cm, will be placed at the centre and edge of the placenta, and the quantitative placental stiffness value was displayed over a B-mode sonogram. The ROI will be placed at homogeneous areas in the axial plane. The centre and edge of the vessel-free placenta away from the cord insertion will be selected as two sampling sites where fetal movements minimally affect the placenta. Five samples were taken from each site, from the centre (sample 1) and edge (sample 2) of the placenta, and will be averaged to obtain samples 1 and 2. In this method acoustic radiation force impulses are used to create shear waves that propagate through tissue. Tracking pulses are used to measure shear wave displacements between two points inside a region of interest (ROI), giving the speed of the shear wave at a certain point. This quantification of the shear wave speed is given in meters per second and, depending on user preference, can be automatically converted to kilopascals by approximating the Young's modulus.

Sample Size

Canan Cimsit et al.1 has reported the mean (SD) SWV to be 2.53 among normal pregnant women and 7.01 among Pre-eclampsia patients. Assuming alpha error of 5% (95% Confidence limit), Assuming a standard deviation of 5 units 12 units in each of the normal group and pre-eclampsia group respectively, Power of 80%.

The minimum required sample size to find the difference in mean SWV between normal pregnant women and Pre-eclampsia patients was 67 patients in pre-eclampsia group and 67 subjects in normal pregnant women group. The total sample size will be 134 subjects.

$$\text{Sample size (n)} = \frac{2S_p^2 [Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}]^2}{\mu_d^2} \quad S_p^2 = \frac{S_1^2 + S_2^2}{2}$$

Where, S_1 : Standard deviation in the normal pregnant women group

S_2 : Standard deviation in the pre-eclampsia group

μ_d : Mean difference between the samples

$1-\beta$: Power

α : Significance level

Statistical Analysis

The current study encompassed both qualitative and quantitative variables. Qualitative variables were expressed as number (%) while quantitative variables were represented by Median (Interquartile Range). The normality of the data was assessed using the Kolmogorov-Smirnov test. Non-parametric Mann-Whitney U tests were employed to compare the two quantitative variables. The Chi-square test and Fisher's exact test were utilized to determine the association between two independent qualitative variables. ROC analysis was employed to determine the cut-off value and assess the accuracy of predicting pre-eclampsia in third trimester of pregnancy. A confidence level of 95% was considered for all statistical tests. Data analysis was conducted using SPSS 20 and R Studio statistical software.

RESULTS

Age Group	Case	Control	Total
18-22	19 28.4%	18 26.9%	37 27.6%
22-27	27 40.3%	26 38.8%	53 39.6%

>27	21 31.3%	23 34.3%	44 32.8%
Total	67	67	134
	100.0%	100.0%	100.0%

Table 1: Group-wise distribution of age between case (N=67) and control (N=67)

$P > 0.05$ (Chi square test)

Table 1: Shows the details of age group classification according to case and control. Out of the total cases highest patients were from the age group 22 – 27 years similarly in the control also the highest patients were observed in the same age group. Age group was not statistically significant with case and control ($P > 0.05$)

Group		N	Median	(IQR)	P-value
E1 (Centre of placenta)	Control	67	3.02	2.70-3.50	$P < 0.001$
	Case	67	10.88	9.75-13	

Table 2: Comparison of SWE values at centre of placenta (E1) between case (N=67) and control (N=67)

Table 2: Illustrates the Comparison of SWE values at centre of placenta (E1) between the control and case groups. The median of centre of placenta (E1) was higher in the case group at 10.88 (9.75- 13.0) compared to the median of the control group at 3.02 (2.70-3.50) with statistical significance ($P < 0.001$).

Group		N	Median	(IQR)	P-value
E2 (edge of placenta)	Control	67	3.04	2.84-3.66	$P < 0.001$
	Case	67	11.07	9.74-13.03	

Table 3: Comparison of SWE values at edge of placenta (E2) between case (N=67) and control (N=67)

Table 3: Illustrates the comparison of SWE values at edge of placenta (E2) between the control and case groups. The median of edge of placenta (E1) was higher in the case group at 11.07 (9.74- 13.03) compared to the median of the control group at 3.04 (2.84-3.66), with statistical significance ($P < 0.001$).

Group	N	Median	(IQR)	P-value
SWE	Case 67	11.07	9.74-13.03	$P < 0.001$
	Control 67	2.90	2.78-3.58	

Table 4: Median SWE values between case and control

Table 4: Illustrates the median of SWE was higher in the case group at 11.07 (9.74-13.03) compared to the median of the control group at 2.90 (2.78-3.58) with statistical significance ($P < 0.001$).

Out Come	Group				Total
	Control		Case		
	N	%	N	%	
Appropriate for gestational age (AGA)	67	100.0%	44	65.7%	111
Small for gestational age (SGA)	0	0.0%	21	31.3%	21
Stillbirth	0	0.0%	2	3.0%	2

Table 5: Details of fetal outcomes between the case and control groups

Fisher Exact test applied (p-value = 0.000000024)

Table 5: presents the details of fetal outcomes within the case and control groups. In the control group, no patients experienced SAG (Small for Gestational Age) or stillbirths. Conversely, in the case group 31.3% and 3% were observed with SAG and stillbirths respectively. SAG and stillbirth were significantly associated with cases.

Test Result Variable (s)	Area under the ROC curve (AUC)	P-Value	Asymptotic 95% Confidence Interval		Cut-off Value	Sensitivity	Specificity
			Lower Bound	Upper Bound			
SWE	0.958	$P < 0.001$	0.913	1.000	4.87	98.5%	92.5%

Table 6: Assess the accuracy of SWE for predicting Pre-eclampsic pregnancies in third trimester and its cut-off value

Table 6: Presents the details of the cut-off values for the SWE to predict the case. ROC analysis was conducted on the SWE to determine the most appropriate cut-offs for predicting pre-eclampsia in the third trimester. Optimal results were observed with a SWE cut-off value of ≥ 4.87 for predicting pre-eclampsia pregnancies in the third trimester.

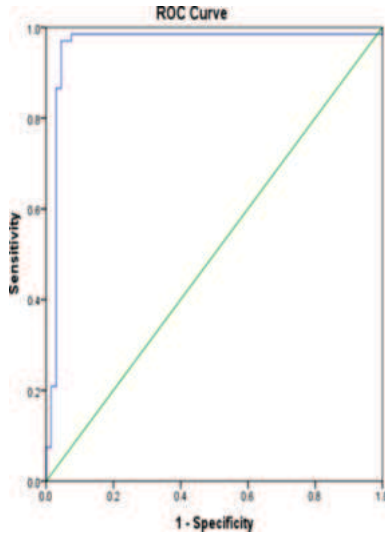


Figure 1: ROC curve constructed to establish the cut-off values for shear wave elastography (SWE) to predict pre-eclampsia

CASE :1. Ultrasound grey scale images from a 21-year-old primigravida at 31 w 2 d gestation.



Figure 2a

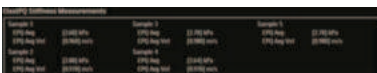


Figure 2b



Figure 2c



Figure 2d

Figure 2: (a) ROI was placed at centre of fundal anterior placenta (b) 5 samples were taken from centre of placenta of placenta in the same patient. The mean placental elasticity value was 2.70 kPa & median value was 2.70 kPa (c) ROI was placed at edge of fundal anterior placenta (d) 5 samples were taken from edge of placenta in the same patient. The mean placental elasticity value was 2.81 kPa & median value was 2.83 kPa. Average SWE is 2.75 kPa (Normal). **CASE 2:** Ultrasound grey scale images from a 32 year old primigravida at 32 W 2 D Gestation with Pre-eclampsia.

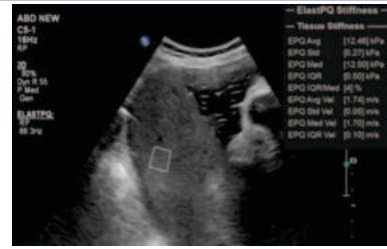


Figure 3a



Figure 3b



Figure 3c



Figure 3d

Figure 3. (a) ROI was placed at centre of fundal placenta (b) 5 samples were taken from centre of placenta of placenta in the same patient. The mean placental elasticity value was 12.46 kPa & median value was 12.50 kPa. (c) ROI was placed at edge of fundal placenta (d) 5 samples were taken from edge of placenta in the same patient. The mean placental elasticity value was 12.78 kPa & median value was 12.80 kPa. Average SWE value is 12.62 kPa (Increased)

DISCUSSION

Screening for preeclampsia based on maternal characteristics and relevant medical history identifies only 35% of patients with PE.¹³ Various maternal serum biochemical indices have been used to predict preeclampsia; however, the predictive value of these indices is low.¹⁴ Initial studies on placental elastography measured the elastic modulus of the human placenta during late pregnancy and found that it was an independent assessment parameter.¹⁵ Currently, shear wave elastography (SWE) is widely used to quantitatively evaluate placental stiffness and has been employed as an adjunct diagnostic tool for various perinatal diseases.¹⁶⁻¹⁸

Additionally, the stiffness of the placenta is regarded as a potential biomarker for placenta-mediated disease detection.¹⁹ In recent years, there have been an increasing number of studies examining the usage of ultrasonic elastography in diagnosing PE. The aim of study was to provide a comprehensive evaluation of the diagnostic performance of ultrasonic elastography in PE.

Out of the total cases in the present study, majority of the patients were from the age group 22 – 27 years. Similarly, in the controls majority of the patients were observed in the same age group. Age group was not statistically significant with case and control ($P > 0.05$). Similar finding was found in the study conducted by Meena, R et al²⁰ on 230 participants between 16 and 20 weeks. The age of the participants ranged from 16 to 35 years. The average age of participants in group B (controls) was 24.89 years, and in group A (cases) was 23.92 years.

In our study, the median of SWE was higher in the case group at 10.98 (9.70-13.13) compared to the median of the control group at 2.90 (2.78-3.58), with statistical significance

($P<0.001$). The median of E1 (center of placenta) was higher in the case group at 10.88 (9.75- 13.0) compared to the median of the control group at 3.02 (2.70-3.50), with statistical significance ($P<0.001$). Median of E2 (edge of placenta) was higher in the case group at 11.07 (9.74-13.03) compared to the median of the control group at 3.04 (2.84-3.66), with statistical significance ($P<0.001$). In the Meena, R.et al²⁰ study, the SWE value of the placenta was calculated from the average of measurements obtained from at least three places: E1 – Right peripheral part of placenta, E2 – Center of placenta and E3 – Left peripheral part of placenta. The average shear modulus value was 2.74 kPa. The average value of placental shear modulus in group B (controls) was 2.51 kPa and in group A (cases) it was 4.61 kPa (p value <0.0001). The average SWE value of the women included in the Vikas Singh et al²¹ study during the initial screening was (10.06 $\pm$ 15.06) at the center of placenta and (10.49 $\pm$ 15.62) at the placental edge. The average elasticity values in both the central (27.98 $\pm$ 16.12 vs. 4.57 $\pm$ 6.57 kPa) and peripheral areas of placenta (29.14 $\pm$ 16.12 vs. 4.80 $\pm$ 7.70 kPa) were significantly elevated as compared to normal pregnancies. The findings in studies conducted by Meena, R.et al and Vikas Singh et al were similar to current study.

In the present study, in the control group, no patients experienced SAG (Small for Gestational Age) or stillbirth. Conversely, in the case group, 31.3% and 3% were observed with SAG and stillbirths respectively. SAG and stillbirth were significantly associated with cases. In the study by Cimsit et al¹, out of 28 cases, 64.2% (18 of 28) were small for gestational age, 3.5% (1 of 28) were stillborn, and 32.1% (9 of 28) were appropriate for gestational age. The findings in studies conducted by Cimsit et al¹ were similar to present study.

In the present study, Sensitivity of SWE was 98.5% and Specificity was 92.5% ROC analysis was conducted on the SWE to determine the most appropriate cut-offs for predicting pre-eclampsia in the third trimester. Optimal results were observed with a SWE cut-off value of ≥ 4.87 for predicting preeclampsia pregnancies in the third trimester. Similar studies were conducted and diagnostic performance of the studies are described below in table 7.

Author	Technique Value	Cutoff Value	AUROC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Spiliopoulos M et al.22	mean SWE value	16 kPa	0.82	75	83	82	76
Alan B et al.12	mean SWV value	1.5 m/s	0.99	91	5	50	33
Sirinoglu HA et al.23	mean SWE value	7 kPa	0.82	89	79	81	88
Fujita Y et al.24	mean SWV value	1.2 m/s	0.91	92	91	40	99
Meena R et al.20	mean SWE value	3 kPa	0.97	92	92	58	99
Kılıç F et al.25	median SWE value	7 kPa	0.90	90	86	82	92
Hefeda MM et al.26	mean SWV value	1.4 m/s	0.91	91	86	73	75

Table 7: The summarized results of comparable studies show the Diagnostic Performance of SWE.

SWE, shear wave elastography; SWV, shear wave velocity; AUROC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value.

Author	Gestational Weeks	Technique	Representative Values	PE Group			Control Group		
				n	PSM	Range	n	PSM	Range
Spiliopoulos M. 22	>20	2D-SWE	Mean	23	22 $\pm$ 3 kPa	NA	24	11 $\pm$ 2 kPa	NA
Alan B. 12	27–35	P-SWE	Mean	42	1.4 m/s	1.3–1.5	44	1.1 m/s	1.00–1.1
Sirinoglu HA. 23	23–37	2D-SWE	Mean	9	6 $\pm$ 2 kPa	2–14	75	9 $\pm$ 3 kPa	3–12
Fujita Y. 24	16–32	P-SWE	Median	13	1.4 m/s	1.1–2.4	208	NA	NA
Meena R. 20	16–20	2D-SWE	Mean	25	5 kPa	NA	205	3 kPa	NA
Kılıç F. 25	23–37	2D-SWE	Median	23	21 kPa	2–71	27	4 kPa	2–14
Hefeda MM et al. 26	>18	P-SWE	Mean	9	2.1 $\pm$ 1.5 m/s	NA	46	0.9 $\pm$ 0.4 m/s	NA
		P-SWE	Mean	46	2.2 $\pm$ 1.5 m/s	NA	94	0.9 $\pm$ 0.6 m/s	NA

Table 8: Placental Stiffness in Preeclampsia and Control Groups of Similar Studies
PE, preeclampsia; PSM, placental stiffness measurement; NA, not available; n, number

CONCLUSION

Diabetic patients with foot complications have a thicker Achilles tendon as compared to those without any foot complications. Non-diabetic controls had a relatively thinner Achilles tendon as compared to both the diabetic groups. The diabetic patients with foot complications had a relatively low Young's modulus compared to those without foot complications, which implies that the AT in patients with foot complications are less elastic as compared to those without foot complications. However, there was no significant difference in the stiffness of AT between non-diabetic controls & diabetic patients without foot complications. Hence, decrease in the elasticity of AT & its thickening in diabetic patients can be an important marker of impending foot complications.

Limitations

Our study included a few additional drawbacks. First, because the maximum entry depth was 8 cm, women whose placentas lay posteriorly were not included to participate in the study. This factor can be interpreted as a technical limitation for the use of shear wave elastography in generalized screening. The lack of a histological evaluation of the placentas is another research drawback. Histopathological analysis could reveal a connection between elastography results and structural alterations in the pathology. Although the standardization of the elastography technique was satisfactory, we did not evaluate interobserver variability because we aimed to minimize repeated examinations of the same fetus. Due to the fixed dimensions of the SWE sample box, information about a small area only could be obtained for the elastographic values.

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