Original Article

Role of Shear Wave Elastography in Assessment of Placental Stiffness of Intrauterine Fetal Growth Restriction

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Abstract

Background: Ultrasound play a crucial part in evaluating both normal and high-risk pregnancy . A new ultrasonographic method called shear wave elastography (SWE) is used to measure the elasticity of soft tissues and provide an accurate representation of their composition. **Objectives:** The purpose of this study is to assess placental stiffness in both growths restricted fetuses and normal fetal growth. **Materials and Methods:** A case-control study that involved 100 singleton pregnant women (fifty fetal growth-restricted pregnant women and fifty normal pregnancies as controls), was conducted at the Ultrasound Clinic at Al-Zahraa Teaching Hospital in Al-Najaf governorate, between December 2022 into December 2023. All pregnant women were in their 3rd trimester. All subjects were examined using the GE LOGIC E9 XD Clear ultrasound system with a convex probe (C1-6 probe) and underwent B-mode ultrasonography, Doppler study, and placental 2D SWE examinations. **Results:** Doppler ultrasound results showed mean S/D (2.30 ± 0.35), RI (0.55 ± 0.08), and PI (0.72 ± 0.05) in normal pregnancies, while S/D (5.34 ± 2.58), RI (0.80 ± 0.09), and PI (1.69 ± 0.46) were found in all fetuses in the growth-restricted group.There was a significant difference in the mean placental SWE values between studied groups, where the highest means were found among pregnant with growth restricted pregnancy (11.25 ± 2.69 KPa) while lowest mean was found among normal pregnant (3.13± 0.24 KPa), sensitivity and specificity were 100% and 100% respectively ,with cut-off value of (5.2 Kpa) that can differentiate between normal and abnormal placentae. Among fetal growth restricted mothers, (N=29) were hypertensive, (N=11) were diabetic, (N=8) hypertensive/ diabetic and , (N=10) non hypertensive non diabetic ,in which placental mean SWE measure (13±2.25 Kpa), (10±2.43 Kpa), (13±2.53 Kpa) and (9±2.75 Kpa) respectively that is of non-significant correlation (P value 0.056). **Conclusion:** Placental stiffness was significantly higher in growth-restricted pregnancy {mainly those who have hypertension and diabetes) than in normal pregnancy. There is a strong correlation between placental stiffness & Amniotic fluid index in addition to placental thickness. No correlation between placental stiffness & Doppler US indices (S\D, RI & PI).

Keyword: shear wave elastography, placental stiffness**,** pregnant, Doppler ultrasound

Introduction

The human gestation period, lasting 40 weeks, starts from the first day of a woman's last menstrual period. Pregnancy can vary by up to five weeks, with multiple pregnancies and assisted reproductive technology. [1] he placenta is the largest fetal organ in pregnancy, responsible for vital functions related to the development and protection of the fetus. [2] In vitro models should consider early placenta development events, including fertilization, zygote division, morula formation, and decidualization, which prepares the uterus for implantation. [3] The placenta consists of chorio-

nic and basal plates, separated by intervillous space. The chorionic plate is dense and includes amnion, main stem villi, and chorionic arteries and veins. Anchoring villi attach to the maternal basal plate. [4,5] Ultrasound is commonly used to evaluate the placenta, a thickened, echogenic tissue rim around the gestational sac, as early as 10 weeks into gestation. [6] The association of ultrasonically detectable placental changes with increasing gestational age was first reported by Winsberg *et al.*, [7]. Strain Elastography (SE) is a real-time sonoelastography technique used to measure the elasticity of tissue and its surrounding areas by measuring the mechanical deformation of structures. [8]. Shear-wave elastography (SWE) uses ultrasound to measure tissue stiffness, generating shear waves and capturing images. Young's modulus is used to convert the speed into kilopascals. [9] Shear-wave elastography (SWE) uses ultrasound to measure tissue stiffness, generating shear waves and capturing images. Young's modulus is used to convert the speed into kilopascals. [10] There are currently no reports that suggest the safety of pregnancy is in danger from acoustic radiation force impulse (ARFI) imaging [11] The thermal index (TI) and mechanical index (MI) of the equipment used in the operation are within the bounds established by the American Institute of Ultrasound Medicine (AIUM), despite the fact that elastic imaging based on radiation force employs a high thermal index (TI) [12] ($TI \leq 0.7$, $MI \leq 1.9$). SWE shields placenta from long-term radiation by generating low-density acoustic radiation, ensuring interval between measure-ments, and should last 15 minutes, as per British Medical Ultrasound Society. [13] Radiation force risks are mitigated by fetal exposure to multiple applications, and further research is needed on sonoelastography security during pregnancy, with a positive association between Doppler indices and SWV [14], Wu et al. [15] measured approximately identical SWVs in normal placentas (1.07, 0.98 ± 0.21 and 0.983 ± 0.260 m/s, respectively) which is equal to (2.99 , 2.74 ± 0.21 & 2.75 ± 0.260 Kpa) using a Siemens (2000 ultrasonic diagnostic) instrument. When Yuksel *et al* [16] employed a French sonographic ultrasonography diagnostic device to evaluate the YM values of normal placentas; their measurements (approximately 6.29 ± 1.16 and 6.42 ± 0.63 kPa) showed no significant differences. Placental elasticity values have been measured using diagnostic ultrasonography, with uniform data and no significant differences in patient ethnicity. Pregnant patients must empty their bladder, breathe, supine, and expose their abdomen before in vivo placental SWE examination. System-specific reference values have been established for chronic liver disease and placental SWE to quantify tissue stiffness and normal placental elasticity. [17] MR imaging offers high soft-tissue contrast resolution but lower spatial resolution than US. Sequences like balanced steady-state free-precession, single-shot fast spin-echo/turbo spin-echo, HASTE, and T2-weighted are used for placenta evaluation. [18] MR imaging, including BOLD, DWI, and ASL, aids in identifying the zonal architecture of the uterus, particularly in cases of morbidly adherent placenta. [19] IUGR refers to a fetus's slower growth due to race and gender, while SGA refers to a newborn's below-the-10th percentile birth weight, requiring risk factors and management. [20] Intrauterine growth restriction (IUGR) fetuses can be asymmetrical or symmetrical, with symmetrical IUGR having poorer mortality and morbidity prognosis due to genetic disorders or infections. Fundal height, measured in centim-eters between 24-38 weeks of gestation, is used to screen for fetal growth below or above the 10th percentile, with a single measurement at 32-

34 weeks being 65-85% sensitive and 96% specific. [21] Maternal obesity and uterine leiomyomas may compromise the accuracy of fundal height measurement as a screening tool, potentially necessitating the use of ultrasonography. [22] The updated Apgar score reporting form necessitates regular scores, resuscitation measures, and a comment box for mentioning factors like maternal medications and resuscitation response. [23] The Apgar score measures neonatal depression symptoms like cyanosis, bradycardia, hypotonia, and apnea, reported at 1 minute and 5 minutes post-birth for all infants and 20 minutes for those with a score below 7. [23] Four biometric measures are commonly used: 1) biparietal diameter, 2) head circumference, 3) abdominal circumference, and 4) femur length. Biometric measurements can estimate fetal weight, which can deviate by up to 20% in 95% of cases, and even more in 5% of cases [24] further testing like amniotic fluid analysis and umbilical artery Doppler blood flow investigations are recommended due to high occurrence of structural and genetic defects. [22] Doppler velocimetry examination, especially of the umbilical artery, can reduce perinatal mortality by up to 29% in cases of fetal growth restriction. [22] This aims of the study to assess the placental stiffness in normal and IUGR fetuses using the SWE technique, assess the factors & confounders that affect fetal growth and study the relationship of Doppler findings with the placental stiffness

Materials and Methods

Study Design and Participants

A case-control study that involved 100 singleton pregnant women (50 fetal growth restricted pregnant cases and 50 normal pregnancy as control), was conducted at the Ultrasound clinic at Al-Zahraa teaching hospital in Al-Najaf governorate, during period between December 2022 to December 2023. Fifty pregnant women, suspected to be with intrauterine growth restriction and 50 pregnant women with normal fetal growth as control with no clinical or sonographic evidence of high risk pregnancy. All pregnant women were in their 3rd trimester. All subjects examined by GE LOGIC E9 XDClear ultrasound system with a convex probe (C1-6 probe) & underwent B-mode ultrasonography, Doppler study and placental 2D SWE examinations.

Statistical analysis

The data was collected and analyzed using SPSS version 27 and the analysis of variance test (T-test) was used to clarify the difference between the arithmetic means of the groups included in the study and to determine the significant differences between them at a probability level of $P \geq 0.05$.

Ethical Approval

The College of Medicine at the University of Al-Kufa ethical committee approved this study's ethical approval, obtaining verbal consent from each patient and control.

Results

Regarding cases of normal pregnancy, the mean mother age of the control group with normal pregnancy was (31.70± 4.54 years), Body mass index was (29.52± 3.75 kg\m²). The mean gestational age was (35.36± 2.28 weeks), the mean amniotic fluid index was (15.09± 3.80 cm). The mean Doppler Ultrasonographic exam findings showed {S\D (2.30± 0.35), RI (0.55± 0.08), PI IV (0.72 ± 0.05) }, all neonates were with normal fetal birth weight (2962.30± 352.17gm), all fetuses in the normal pregnant cases were (>10th - < 90th growth percentile),

with normal head circumference to abdominal circumference ratio, normal placental thickness, all neonates were discharged without admission to the neonatal intensive care unit. While pregnant women with growth restricted fetuses, the mean mother age was (35.74± 5.02 years), body mass index was (28.74± 3.84 kg\m²) , the mean gestational age was (29.68 ± 2.05 weeks) ,the mean amniotic fluid index was (3.95± 2.11 cm), the mean Doppler ultrasonographic exam findings showed { S\D(5.34± 2.58) ,RI (0.80 ± 0.09), PI (1.69± 0.46)}.

Table 1: The mean differences of Doppler indices between IUGR and control group (N=100).

Study variables	Study group		Total (N=100)	P value
	IUGR (N=50)	Control group (N=50)		
S/D ratio	5.34±2.58	2.30±0.35	3.82±2.39	< 0.001*
RI	0.80±0.09	0.55±0.08	0.67±0.15	< 0.001*
PI	1.69±0.46	0.72±0.05	1.20±0.59	< 0.001*

Fetal birth weight was (1591.46± 265.93 gm) ,all fetuses in the growth restricted group have (head circumference\abdominal circumference >1.3), majority of fetuses (N=40) are (< 10th growth percentile), (N=10,) are (10th-90th growth percentile), markedly decreased placental thickness, mean Apgar score was (5.78 ± 1.65) in 1minute, majority of neonates was moderately depressed who are admitted to the neonatal intensive care unit (Table 2).

Table 2: The comparison between IUGR and control group according to study variables (N=100)

Study variables	Study group		Total (N=100)	P value
	IUGR (N=50)	Control group (N=50)		
Gestational age at time of scan (weeks)	29.68±2.05	35.36±2.28	32.52±3.58	< 0.001*
Estimated fetal weight (gram)	1442.52±299.7	2658.22±567.3	2050.37±759.6	
Birth weight (gram)	1591.46±265.9	2962.30±352.1	2276.88±755.6	
Apgar score				
Severely depressed	4(8)	0(0)	4(4)	< 0.001*
Moderately depressed	28(56)	0(0)	28(28)	
Excellent condition	18(36)	50(100)	68(68)	
Total	50(100)	50(100)	100(100)	
Growth percentile				
< 10th	50(100)	0(0)	50(50)	< 0.001*
1oth -90th	0(0)	50(100)	50(50)	
> 90th	0(0)	0(0)	0(0)	
Total	50(100)	50(100)	100(100)	
HC/AC				
<1.3	10(20)	50(100)	50(50)	< 0.001*
>1.3	40(80)	0(0)	50(50)	
Total	50(100)	50(100)	100(100)	
Type of labor				
Normal vaginal delivery	34(68)	32(64)	66(66)	0.673
Caesarian section	16(32)	18(18)	34(34)	
Total	50(100)	50(100)	100(100)	

There was a significant difference in the mean placental SWE values between studied groups, where the highest means were found among pregnant with growth restricted pregnancy (11.25 ± 2.69 KPa) while lowest mean was found among normal pregnant (3.13± 0.24 KPa), sensitivity and specificity were 100% and 100% respectively, with cut-off value of (5.2 Kpa) that can differentiate between normal and abnormal placentae.

Table 3: The mean differences of mean SWE between IUGR and control group (N=100)

Study variables	Study group		P value
	IUGR (N=50)	Control group (N=50)	
Mean SWE	11.25±2.69	3.13±0.24	< 0.001*

Among fetal growth restricted mothers, (N=29) were hypertensive, (N=11) were diabetic, (N=8) hypertensive/ diabetic and, (N=10) non hypertensive non diabetic, in which placental

mean SWE measure (13±2.25 Kpa), (10±2.43 Kpa), (13±2.53 Kpa) and (9±2.75 Kpa) respectively that is of non-significant correlation (P value 0.056). Among the growth restricted pregnant women, there was a significant strong and positive correlation between amniotic fluid index and placental stiffness values but no significant correlation between SWE & study variables (Doppler US findings, gestationalage and birthweight).

Table 4: The correlation between SWE - E median and study variables including (gestational age, birth weight and amniotic fluid index) among pregnant women with IUGR (N=50).

Study variables	P value
Gestational age (weeks)	0.26
Birth weight (gram)	0.215
Amniotic fluid index	< 0.001*
Placental thickness	< 0.001*

Illustrated cases

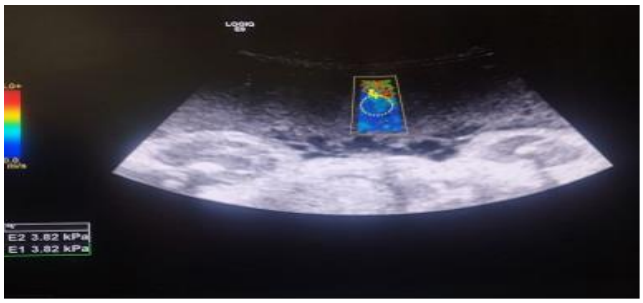

Figure 1: 30 year's old pregnant lady, not hypertensive, not diabetic, gestational age 37 weeks, ROI in the central fetal coloured area, mean elasticity value 3.8 Kpa.

Figure 2: 35 year's old pregnant lady with FGR, hypertension, gestational age 34 weeks, ROI in the central fetal coloured area, mean elasticity value 6.97Kpa.

Discussion

SWE is a state-of-the-art technique that has been discovered for assessing different organs stiffness and their associated illnesses. [25,26] SWE is a non-invasive method that is less operator dependent compared with strain elastography which depend on dynamic compression. [27,28] This study is the one that uses SWE to target placental elasticity in the third trimester of pregnancy in both the normal and FGR pregnant women In which 50 normal healthy pregnant participants, none of them have hypertension, nor diabetes mellitus, no one of them are smokers, two out of 50 cases have positive obstetric history of IUGR, no significant past history of abortions, fetal growth percentile more than 10th and less than 90th growth percentile, HC/AC was less than 1.3, the fetal Apgar score was more than 7 in 1 and 5minutes in all fetuses comparable to previous study by Levy *et al* ., [25] that show mean Apgar score (7.1 ±2.3) in 1minute and (8.4 ±1.2) in 5 minutes. Regarding the placental stiffness, the mean value of SWE in the control cases (3.13± 0.24 Kpa) which is comparable to Khanal *et al* ., [26] that show mean SWE value (3.38 Kpa) in the control cases while a study by Li *et al*.,[29] the average value of elastic modulus was (7.60 ± 1.71 kPa) for placental edge and (7.84 ± 1.68 kPa) The study found higher elasticity values in normal pregnant women's central placenta, suggesting varying tissue calcification degrees could affect late pregnancy elasticity, requiring further exploration. The study by Joshi *et al*., [30] also found the mean elasticity values in the central and the peripheral part of the placentas of control cases to be (5.47 ± 1.74 and 5.23 ± 1.31 kPa), respectively. However, most other studies have shown mean placental elasticity values

comparable to our study in normal pregnancy. [31] Another study by Quarello *et al*., [28] slightly lower mean placental elasticity values of (2.28 kPa) at the center of the placenta and 2.48 kPa at the edge. The proper cutoff value for a normal placenta is called into doubt by these findings across several investigations. Disagreement in research about the placenta's altered SWE value with POG further exacerbates this issue. In a study by Wu *et al*.,[15] 50 singleton healthy pregnant women in their second-trimester and 50 healthy singleton pregnant women in their third-trimester showed no significant difference between the second- and third-trimester placental shear wave velocity. Study by Ohmaru*et al.,* [32] also failed to show correlation between SWE value and gestational age. In the current study, 50 pregnancies with a diagnosis of asymmetrical IUGR (based on LMP, 1st US exam & the current US with EFW measurements, HC/AC), about 15 cases were symmetrical IUGR are excluded from the study to avoid misinter-pretation as small for gestational age. Significant past obstetric history of abortions, all of the 50 cases with IUGR have HC/AC >1.3, majority of fetuses (N=40) are (< 10th growth percentile), (N=10) are (10th -90th growth percentile). Apgar score of IUGR neonates was (5.78 ± 1.65) in 1min & (6.55 ± 1.66) in 5 minutes ,majority of neonates (N=28) was moderately depressed (Apgar score 4-6) comparable to Sridhar *et al.,* [33] that show significant low Apgar score in IUGR fetuses ,mean Apgar score 1- minute [3] and 5-minute [34] and comparable to Levy *et al.,* [25] that show Apgar score less than 7 in 1and 5 minutes. The current study has shown that the mean value of placental stiffness in pregnant with IUGR was (11.25 ± 2.69Kpa) and this result was in concordance with Quibel*et al* ., [35] whom found the mean SWE value (11.7 ± 1.5 KPa). 29 out of 50 of FGR cases were hypertensive , 11 out of 50 are diabetic, 8 out of 50 are (hypertensive and diabetic) and 10 out of 50 are non-hypertensive non diabetic, mean placental stiffness were (13 ± 2.25 Kpa), (10 ± 2.43 Kpa), (13 ± 2.53 Kpa) and (9 ± 2.75 Kpa) respectively, (P value 0.056), non significantcorrelation that is comparable to the study done by HU *et al* ., [17] who investigate placental stiffness of pregnancy with preeclampsia, FGR and healthy pregnancy who found that significant difference (3.6 Kpa) between PE and FGR group, while (9.45 Kpa) difference between PE and healthy group, this finding was comparable to Anuke*et al* ., [36] the mean SWE values were significantly higher in PE and FGR groups in which mean values of SWE is (14 ± 5.95Kpa). A new study by Arioz Habibi *et al*., [37] they found the placentae of IUGR pregnancies show median elasticity values of the central part of the placentas (28kPa) and fetal sides (21.5 kPa) ,median elasticity values of peripheral part of placentas from maternal (22kPa) and fetal sides (22.5 kPa),were significantly higher in IUGR pregnancies compared to the control group ($p < 0.001$) this result show higher measurement than our study, they may be due to their small sample size. Higher result also seen by Deeba *et al.,* [38] where the mean value of SWE (15.30 ± 2.96Kpa) while Akbas *et al* ., [39] show mean value of SWE (5.5 ± 2.09Kpa) using pSWE (Philips health care) and Khanal *et al.,* [26] Show lower mean placental stiffness among IUGR pregnancies which is about (3.85 kPa). Our result represents middle level neither too high nor too low, this may be due to the selection of ROI site, and we try to select more homogeneous placental tissue in the center of placenta. Furthermore, research has demons-trated strong inter- and intraobserver variability in SWE measurement, which runs counter to the

previously mentioned findings [40]. Previous studies indicate that demographic variations and measurement techniques may influence IUGR prediction, but no prior evaluation has evaluated their ability to predict IUGR earlier. [41] Research on the potential impact of maternal hypertension-induced elevated internal tissue pressures on placental stiffness is comparatively lacking [42, 43].The accuracy of USG SWE as a test for IUGR prediction presents the next challenging circumstance as the readings above 5 Kpa are borderline. Measurement of SWE values can be improved by avoiding fetal movement and shallow breathing, as these factors can reduce measurement errors. [32] The study revealed that placental thickness in growth restricted pregnant women is lower than normal women's, and it strongly correlates with SWE in these women. This in line with Altunkeser*et al.*, [44] attributed to the placental infarction, sclerotic narrowing of the arteries and villous inflammation that were demonstrated histo-logically in preeclamptic and diabetic pregnant women's placentas. There was significant correlation in our study between mean SWE value and AFI in IUGR cases .This result was also revealed by Khanal *et al.,* [26] who found a significant correlation between AFI and mean SWE value and Edward *et al*., [11] who found that AFI , to be significant predictor of placental elasticity. Another crucial instrument that is regularly employed in the management of IUGR is the UA Doppler indices. In this study, UA Doppler indices showed no significant positive correlation with mean SWE values in IUGR cases comparable to Ohmar *et al*., [32] who did not found any association with UA RI, while Khanal *et al.,* [26] show significant positive correlation between SWE & Doppler indices. Based on the results of the present study, the cutoff value of mean SWE for prediction of IUGR pregnancy was (≥ 5.20Kpa) The sensitivity was 100.0% and specificity was 100.0% of SWE to predict IUGR which was high, could be due to limited sample size in our study with the complementary Doppler study indices (S/D ratio & RI) showed sensitivity 96.0% and specificity 100%. Recent results of Hefeda*et al* ., [45] the cutoff value for prediction of preeclampsia and/or growth restriction was 1.35 m/s (=3.77Kpa) with sensitivity, specificity were 91.3%, 86.4%. In our study (in IUGR cases) the sensitivity was 100.0% and specificity was 98.0% of Amniotic fluid index as the vast majority were oligohydramnios nearly comparable with Sonia *et al.,* [46] that showed that clinical estimation of liquor has a sensitivity of 74.35 % and a specificity of 90.16% . Further research is needed to understand the potential role of SWE in managing and forecasting IUGR patient outcomes, as current data is insufficient, and Doppler results are not diagnostic. [47]

Conclusion

Placental stiffness was significantly higher in growth-restricted pregnancy {mainly those who have hypertension and diabetes) than in normal pregnancy. There is a strong correlation between placental stiffness & Amniotic fluid index in addition to placental thickness. No correlation between placental stiffness & Doppler US indices (S\D, RI & PI)

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