Research Article

Comparison of Placental Elasticity and Different Spectral Doppler Indices in Normal and Intrauterine Growth Restricted Fetuses

Sabar Butt[1], Syed Amir Gilani[2], Asif Hanif[3], Syeda Khadija[4], Raham Bacha[5]

[1,4,5] University Institute of Radiological Sciences, University of Lahore, Pakistan; [2,3] University Institute of Public Health, University of Lahore, Pakistan

Abstract:

Objective: Comparison of Placental Elasticity and different spectral Doppler indices in normal and intrauterine growth restricted fetuses to establish efficacy of shear wave elastography in early detection of Intrauterine Growth Restricted (IUGR).

Design: Cross sectional comparative. 290 pregnant women previously diagnosed by ultrasound as normal and intrauterine growth restriction fetuses which were included in this study, placental elasicity in both groups was evalauted by SWE (shearwave elastography) and compared.

Methods: Primarily both groups were scanned for grayscale and Color Doppler ultrasonography in which we took the measurements of resistivity and pulsatility indices of umbilical artery (UA), uterine artery and MCA (middle cerebral artery). In these groups placental elasticity was evaluated by SWE .The ratios of strain were compared between both groups. Statistical study was carried out by using Mann-Whitney test. Cut-off values for elasticity were analyzed by plotting receiver operative characteristic curve (ROC), sensitivity. Specificity and DA (diagnostic accuracy) for IUGR were designed established on Shear wave elastography measurements.

Results: The mean placental elasticity in intrauterine growth restriction (IUGR) and in normal groups was 28.71+7.28 and 5.64+1.53, respectively while in the IUGR group median placental elasticity was 27+7 and 5.50+2 with statistically elevated median among patients in the IUGR group ($P<0.001$).

Conclusion: Among IUGR feasts, the values of placental stiffness are very high; SWE can be utilized for IUGR early detection like a non-invasive, auxiliary tool for gray-scale and color Doppler.

Corresponding Author | Dr. Sabar Butt, University Institute of Radiological Sciences, University of Lahore, Pakistan
Email: arsamali@hotmail.com

Key words: SWE, IUGR, Placental Elasticity(kpa), MCA, Umbilical artery, Uterine artery, pulsatility index, resistive index.

Introduction:

The incapability of the fetus to attain its genetic determined potential growth element is the IUGR and denotes the foremost basis for intrauterine fetal demise (60-70%)[1.] The abnormal fetal growth is demarcated as weight of fetus underneath the tenth percentile (or <2SD) than mean for GA (gestational age). The end-point weight for this is 2500g[2]. Asymmetric IUGR is observed after twenty eight weeks. This is the 2nd significant cause for perinatal death after the prematurity (41 percent)[3]. The complications for instance: stillbirths, hypothermia, hypoglycemia, birth hypoxia, necrotizing enterocolitis, pulmonary hemorrhages, deficient cerebral function and impaired neuro development during babyhood are faced by fetuses together with growth retardation. They as adults are at enhanced risk of type 2 diabetes, hypertension and heart diseases[4]. Each year among thirty million FGR (fetal growth restriction) infants, 75 percents are born in the Asian countries, mostly in the South Central Asian countries. Where thirty percent African children are found underweight, matching figure for South Asian countries is above 50 percent. It was evident from a study carried out in Karachi that FGR incidence was 24.4 percent in 738 singleton deliveries. In Pakistan the IUGR prevalence is 25 percent[8-5]. The IUGR could occur at any time after twenty weeks of the gestation. Gestational age is strongly related to the intensity of fetal impairment at the onset of preeclampsia (PE). There are anomalous uterine artery Doppler judgments, FGR, unfavorable maternal & neonatal outcomes in early onset of preeclampsia at or before 34 weeks[6]. Early documentation of patients who are at an enhanced risk of preeclampsia is hence most significant for assessment and precautionary management to enhance maternal & perinatal outcomes. Sign of utilizing uterine artery Doppler like a part of common sonographic test was based on the reality of inadequate uteroplacental perfusion during preeclampsia[7]. The persistence of post systolic notches in bilateral uterine arteries and raised pulsatility index values of the uterine arteries in the second trimester, were stated as valuable prediction regarding preeclampsia. The studies scrutinizing the predictive accuracy of uterine artery publicized low positive predictive values (PPV) of the uterine artery Doppler indices[8]. For the detection of preeclampsia, sensitivity of Doppler measurements was marginally upgraded by combi-nation of Pulsatility index (PI) along with most favorable biological markers.[9] A newly established ultra-sound imaging technology is elastography, the elementary principle of which is to enforce an internal/ external dynamic or the static excitation on any tissue so that this tissue will respond to displacement, velocity, or strain, among others[10]. This elasticity imaging procedure can be used to evaluate tissue elastic modulus directly or indirectly[11]. This study was aimed to establish the role of shear wave elastography in early recognition of IUGR fetuses by a single step, irrespective of traditional ultrasonographic criteria including fetal biometry and different Doppler indices.

Methods:

This Cross sectional comparative study was undertaken at Sabiry color Doppler Ultrasound centre, Faisalabad after obtaining approval from institutional ethical committee. Our sample size was 290 with 50% was in group 1 (NORMAL) and 50% was in group 2 (IUGR). From each group 145 patients were s elected by systematic random sampling. Study Duration was 18 months. We included Singleton pregnancy, Primigravida and multigravida, Diagnosed cases of IUGR by color Doppler study, anterior placenta included and fetal anomalies, Posterior placenta, Non-Cooperative individual excluded from the study. The patients having placenta in posterior location were also excluded as the detection depth of the ultrasound transducer is 8cm.

Group 1: Spectral Doppler findings and placental elasticity with normal fetus at 24 to 36 weeks of gestational age.

Group 2: Spectral Doppler findings and placental elasticity with IUGR fetuses at 24 to 36 weeks of gestational age. Primarily basic grayscale and Doppler ultrasonography with measurements of UA, middle cerebral artery and uterine artery resistivity as well as pulsatility indices of both groups performed. Subsequently placental elasticity was evaluated by SWE in both groups. Between both groups strain ratios were compared. Statistical study was carried out by using Mann-Whitney test (as data was not normal) was applied to compare median of quantitative data in both groups. Cut-off values for elasticity were analyzed by plotting ROC curves.

Obstetrical and Doppler sonography and elastography were accomplished with an Aplio 500 platinum (canon medical systems) equipped with a shear wave– elastography. The shear wave elastography is an ultra-sound elastographic technique in which shear waves propagate through in real time , is quantitative and user independent. After getting informed written approval form, the data was gathered by researcher himself using developed structured questionnaire. Doppler and elastography scans were completed in the same session.

Results:

All variables were not normally distributed on applying Kolmogorov-Smirnov and Shapiro-Wilk, p-value < 0.001. The mean age of all females was 27.98 ± 5.17 years while 30.96 years among females in IUGR group and 25.03 ± 4.10 years in normal group. The median age of females in IUGR group was 32 ± 6 years was statistically higher as compared to normal group (24.50 ± 6 years), p-value <0.001. The mean GA of IUGR group was 30.24±2.75 weeks while 32.41±2.82 weeks in normal group. Likewise median gestational age was found statistically lower in IUGR group (30.24 ± 2.75 weeks) when compared with normal group (32.41 ± 2.82 weeks), p-value < 0.001. The average uterine artery resistance index (RI) in IUGR group was 0.70±0.08 and in normal group was 0.42±0.05 while median uterine artery resistance index in IUGR group was 0.695±0.12 and among patients in normal group was 0.42±0.08, respectively with statistically higher values of uterine artery resistance index in the IUGR group, p-value <0.01. The mean uterine artery PI among patients in the IUGR group was found 1.93±0.79 and among patients in normal group was 0.67 ± 0.12 while the median uterine artery PI (UAPI) in the IUGR group was 1.76±0.99 and in normal group 0.66 ± 0.15 with statistically higher uterine artery PI values in IUGR group, p-value < 0.01. The average UA SD in the IUGR group was 2.34±3.99 and in the normal group was 2.41 ± 052 while the median umbilical artery SD in IUGR group was 3.67 ± 1.23 and in normal group was 2.43 ± 0.73 respectively with statistically higher lower umbilical artery SD values in IUGR group, p-value < 0.01. The mean UAPI in the IUGR group was 2±1.45 and among patients in the normal group was 0.87±0.24 while the median UAPI in the IUGR group was 1.47±0.58 and among normal women was 0.87±0.32 respectively with statistically higher umbilical artery PI values in IUGR group, p-value < 0.01. The average middle cerebral resistance index was 0.62±0.05 in the IUGR group and was 0.74±0.05 among normal females, the median middle cerebral resistance index was 0.61±0.08 in the IUGR group and 0.75±0.09 among normal women with statistically lower middle cerebral RI in IUGR group, p-value < 0.001. The average middle cerebral Pulsatility Index was 1.15±0.26 in IUGR group and 1.63±0.36 in normal group while median middle cerebral PI was 1.12 ± 0.36 in IUGR and 1.62 ± 2.54 in normal group with statistically lower middle cerebral PI in IUGR group, p-value < 0.001. The average placental elasticity among women in IUGR group was 28.71±7.28 and in normal group was 5.64±1.53 while median placental elasticity among women in IUGR group was 27±7 and among normal women was 5.50±2 with statistically significant median among patients in IUGR group (P<0.001. Test result variables area at 0.55 uterine artery cut-off value of resistance index sensitivity was 100 percent while specificity was 99.3 percent, PI of uterine artery cut off value was 1.1 and sensitivity 100% and specificity 89.3% umbilical artery S/D ratio was 3.1 and sensitivity 94% and specificity 71%. MCA RI = 0.66, sensitivity 86 percent and the specificity 76% MCA PI=1.27 sensitivity 88% and specificity 74% respectively has been specified by correspondent analysis using cutoff value of elasticity 15 kPa with sensitivity 100% and specificity 100%.

Table -1: *Normality testing of all variables*

	Kolmogorov-Smirnov			Shapiro-Wilk			Distribution
	Statistic	d.f	p value	Statistic	d.f	p value	
Age (years)	0.094	300	<0.001	0.971	300	<0.001	Non-normal
Gestational age (weeks)	0.076	300	<0.001	0.967	300	<0.001	Non-normal
Uterine artery RI	0.155	300	<0.001	0.938	300	<0.001	Non-normal
Uterine artery PI	0.177	300	<0.001	0.833	300	<0.001	Non-normal
Umbilical artery SD	0.296	300	<0.001	0.755	300	<0.001	Non-normal
Umbilical artery PI	0.256	300	<0.001	0.625	300	<0.001	Non-normal
Middle cerebral RI	0.094	300	<0.001	0.974	300	<0.001	Non-normal
Middle cerebral PI	0.054	300	0.037	0.974	300	<0.001	Non-normal
Placental Elasticity (kpa)	0.245	300	<0.001	0.858	300	<0.001	Non-normal

Table -2: *Comparison of various variables in both study groups (IUGR versus Normal)*

	Groups	Mean	S.D	Median	IQR	Z[a]	p-value
Age (years)	IUGR (n=150)	30.93	4.40	32.00	6.00		
	Normal (n=150)	25.03	4.10	24.50	6.00	-9.91	<0.001
	Total (N=300)	27.98	5.17	28.00	9.00		
Gestational Age (weeks)	IUGR (n=150)	30.24	2.75	30.10	4.20		
	Normal (n=150)	32.41	2.82	33.0	3.52	-6.66	<0.001
	Total (N=300)	31.33	2.99	31.6	4.30		
Uterine artery RI	IUGR (n=150)	0.70	.08	0.695	0.12		
	Normal (n=150)	0.42	.05	0.42	0.08	-14.96	<0.001
	Total (N=300)	0.56	.15	0.54	0.28		
Uterine artery PI	IUGR (n=150)	1.93	.79	1.76	0.99		
	Normal (n=150)	0.67	.12	0.66	0.15	-14.77	<0.001
	Total (N=300)	1.30	.85	0.96	1.11		
Umbilical artery SD	IUGR (n=150)	2.34	3.99	3.67	1.23		
	Normal (n=150)	2.41	.52	2.43	0.73	-7.82	<0.001
	Total (N=300)	2.37	2.84	2.78	1.64		
Umbilical artery PI	IUGR (n=150)	2.00	1.45	1.47	0.58		
	Normal (n=150)	0.87	.24	0.87	0.32	-12.25	<0.001
	Total (N=300)	1.44	1.19	1.10	0.67		
Middle cerebral RI	IUGR (n=150)	0.62	.05	0.61	0.08		
	Normal (n=150)	0.74	.05	0.75	0.09	-12.34	<0.001
	Total (N=300)	0.68	.08	0.68	0.15		
Middle cerebral PI	IUGR (n=150)	1.15	.26	1.12	0.36		
	Normal (n=150)	1.63	.36	1.62	2.54	-11.10	<0.001
	Total (N=300)	1.39	.39	1.36	0.54		
Placental Elasticity (kpa)	IUGR (n=150)	28.71	7.28	27.00	7.00		
	Normal (n=150)	5.64	1.53	5.50	2.00	-15.02	<0.001
	Total (N=300)	17.17	12.69	15.00	21.75		

[a]: Mann-Whitney Test was applied

Discussion:

This research showed significantly higher placental stiffness in preeclampsia patients. And it was found that the placental elasticity was strongly correlated with the Doppler indices of umbilical artery, uterine artery and middle cerebral artery. Based upon elastography the imaging systems have established generous consideration in current years for non-invasive evaluation for mechanical properties of tissue. To produce qualitative and quantitative data useful for analytical purposes, variations in elasticity of soft tissue in several pathologies are used[12]. After mechanical force (compression/ shearwave) application, the tissue stiffness reaction is measured in dedicated imaging modes. As these are ultrasound based approaches and of precise attention due to so many integral benefits such as widespread accessibility even at the bedside and comparatively low cost[13]. Various excitation methods have been developed using multiple elastographic techniques. Elastography has shown advantageous results for evaluation of fibrotic changes in liver. Fresh applications in kidney, lymph node, prostate, thyroid and breast scan are evolving[14].

SWE showed that breast nodules having malignant tissues have higher elasticity values (Kpa) and are rigid and stiff because of escalated number of malignant cells and persistent growth of dense fibrous tissue adjacent to the tumor. Several studies have established the role of elastography in assessment of liver fibrosis, which has minimized the requirement for liver biopsy[15,16].

Li et al[17] argued in his research that for identification of preeclampsia, 7.35 kPa is the mean stiffness value, with 90 percent sensitivity & 86 percent specificity. In healthy control group the diastolic nicks were not detected and had 100% specificity. The early diastolic nick existence among patients directed to 56.5% sensitivity. The rates of sensitivity, specificity, PPV & NPV as 91.3 percent, 92.6 percent, 91.3 percent and 92.6 percent, respectively have been indicated by complementary study utilizing cutoff value 7.35 kPa with existence of uterine artery nick. Our results are compatible with Li et al. Our results Test result variables area at 0.55 uterine artery cut-off value of the RI sensitivity was 100 percent while specificity was 99.3 percent, PI of uterine artery cut off value was 1.1 and sensitivity 100% and specificity 89.3% umbilical artery S/D ratio was 3.1 and sensitivity 94% and specificity 71%. MCA RI = 0.66, the sensitivity 86 percent and the specificity 76 percent MCA Pulsatility Index was 1.27 along with 88 percent sensitivity and 74 percent specificity has been specified by correspondent analysis using cutoff value of elasticity 15 kPa with sensitivity 100% and specificity 100%.

Hatice Arioz Habibia[18] indicated in his research that patients in IUGR group showed considerably higher median values of placental stiffness as compared to control group. Elasticity values from the central and peripheral maternal surface of placenta were taken and found a median of 28kPa and 21.5kPa among patients in IUGR group, whereas 6kPa and 5.35kPa among normal women, respectively (P<0.001). Fetal placental central and peripheral surfaces had a median of 22kPa and 22.5kPa in IUGR group while 5kPa and 5.30kPa in among normal females, respectively (P<0.001) .These are strongly related with our results.

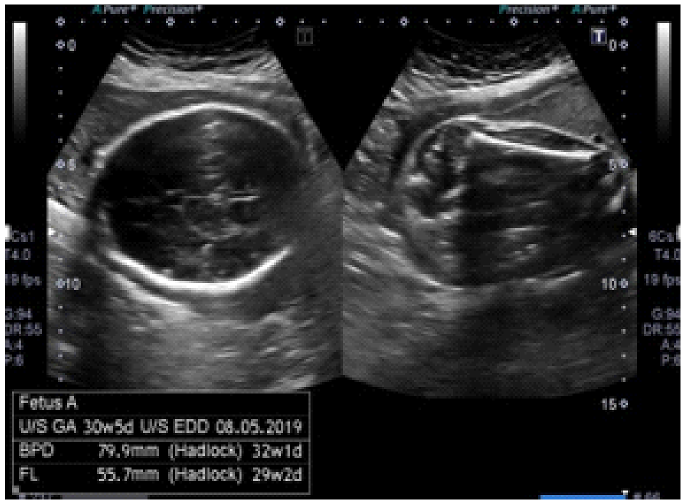
The study of Murat Akbas[19], used ROC curve in enlightening the ideal value of placental elasticity to identify the IUGR. To differentiate between healthy and malfunctioning placentation, 3.86kPa was the cut-off value while 86% and 56% were the sensitivity and specificity, respectively. This study is strongly related with our study. Evaluation of shear wave elastographic values in several groups of the pregnant females was done by Ohmaru et al. and Alan et al33 and initiated statistically considerable differences in the SWS between females who had normal pregnancy (n ¼ 143), hypertension (n ¼ 15) and FGR (n ¼ 21), together with SWS 0.98 þ 0.21, 1.60 þ 0.45 m/s and 1.28 þ 0.39, respectively. Likewise, Alan and colleagues testified elevated SWS among females with preeclampsia (n ¼ 42) when compared to those who had normal gestation (n ¼ 44). The mean values of SWS were 1.39(1.32e1.53) vs 1.07 (1.00e1.14), (P<0.001)

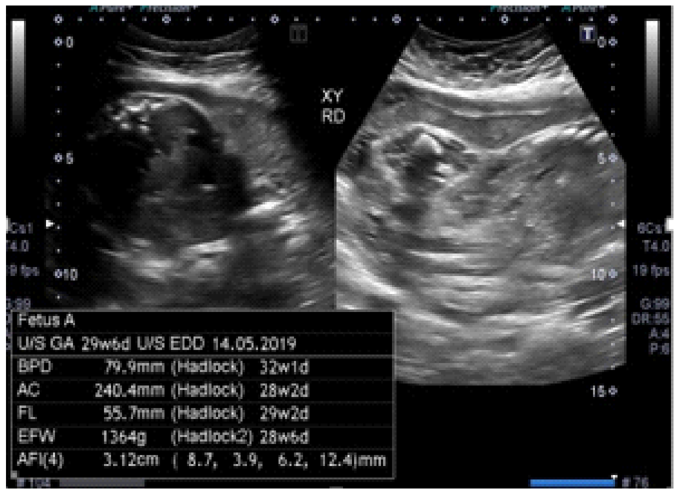
Daniel Wilhelm20 studied elastographic application in uncomplicated pregnancies vs IUGR+PE. This research at derived that in IUGR + PE cases, the stem villus vessels along with elastic tissue fibers were minute (B; P=0.00096, or were observed in segments in IUGR + PE (E; P<0.00001), whereas there were numerous elastic tissue fibers in stem villi in normal pregnancies. There were much more blood vessels with no any elastic tissue fibers in cases of IUGR + PE (A; P=0.0031). This study is also co related with our research. Hasan Eroğlu[21] compared placental elasticity among IUGR and normal pregnancies by the ex vivi strain elastography. They found that the Placental elasticity was increased in women with preeclampsia that progresses due to the comparable reasons with IUGR. It was revealed that in the prompt identification of preeclampsia, placental elasticity could be used. Placenta strain ratio (PSR) was 1.3 and 2.8 in control and IUGR groups, respectively. Thus statistically major difference between both groups regarding placental elasticity was found (P<0.001). The area under the curve was 0.90 in ROC scrutiny to define cut-off point concerning PSR value. Fahrettin Kılıç[22] utilized SWE in judging placenta in preeclampsia and found the best noteworthy stiffness mean value for finding of PE was 7.35kPa, with 90 percent sensitivity and 86 percent specificity. Post systolic notches were not recognized among healthy controls and had 100.0 percent of specificity. The patient group presented with diastolic notches with sensitivity of 56.5%. The rates of sensitivity, specificity, PPV and NPV as 91.3 percent, 92.6 percent, 91.3 percent and

92.6 percent, correspondingly has been designated by complementary analysis utilizing cutoff value of 7.35 kPa with the presence of early diastolic notch[23].

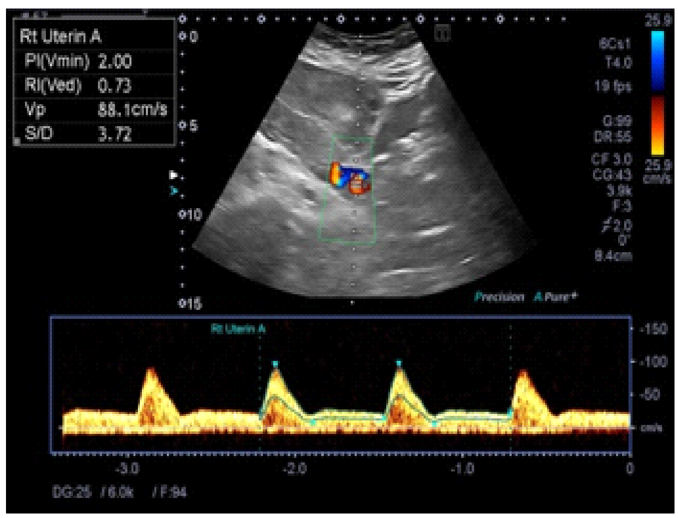
Sugitani[24] et al. studied that the elastography device's acoustic output, thermal and mechanical indices are within established safety ranges. No thermal or mechanical structural changes were found in full term delivered placenta, which defines that there is no biological effects of the acoustic radiation force impulse imaging on placenta. Issaoui et al[25] endorsed that elevated intensity of US can be utilized for the inspection of fetus because amniotic liquid neither attenuate ultrasonic waves nor transmit push wave. The monitoring fetal growth in the womb has always been a mystery and as hypotrophic fetuses are the major cause of fetal morbidity and mortality, therefore extensive surveillance of such fetuses is required as compared to the surveillance of journal pregnant population. The eagle's eye on such fetuses is also necessary not only to manage growth but to find the best time and method for delivery to secure fetuses and ensure mother's life. In current era fetal growth monitoring done by repeated ultrasound exams measuring fetal biometry, biophysical profile, Doppler indices of umbilical artery, uterine artery and middle cerebral arty. Furthermore MRI to access placental function is used as well. More over positron emission tomography for placental function offering useful metabolic and functional data also helpful to investigate the placental function, fetal metabolism and to access fetal hypoxia. As all above mentioned techniques are not only time consuming, hectic or have hazardous effects of radiation to mother and fetus. Therefore this situation was evolving the attention of the researches to adopt such technology to access placental function which should be single step, and had no harmful effects to mother and fetus as well. As placental SWE is a new technique which is non-invasive, quantitatively evaluate placental elasticity and is operator independent therefore assessment of placental elasticity by SWE vs Doppler studies in hypotrophic fetuses from 24-36 weeks of gestation will establish the role of shear wave elastography as placental shear wave elastography single step diagnostic tool in early detection of hypotrophic fetuses. This study will open up the doors for early detection of IUGR and management will be easy.

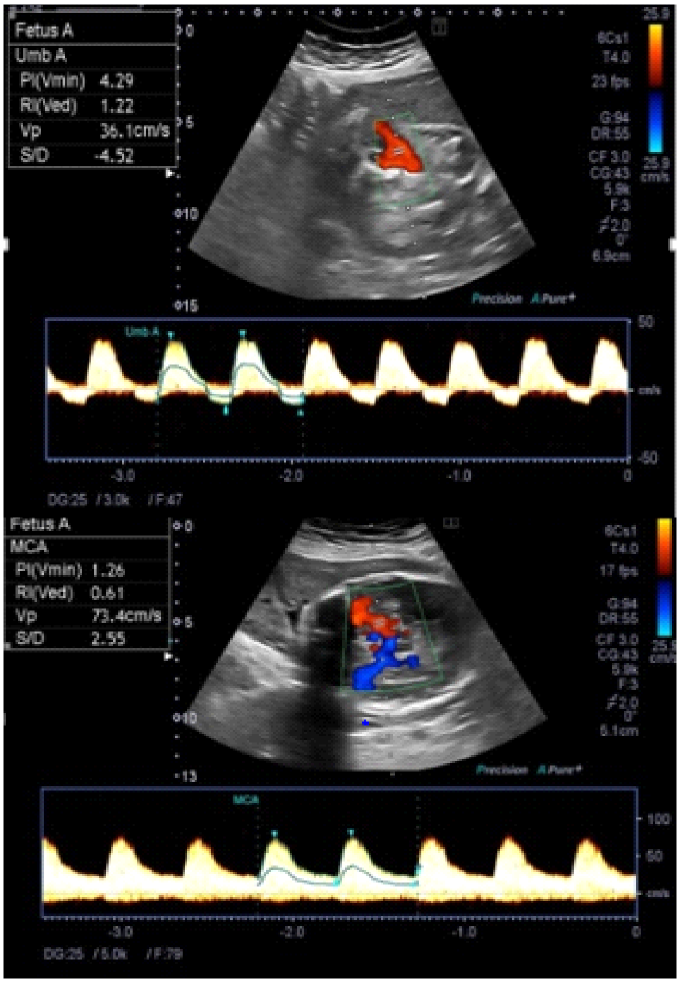
Images:



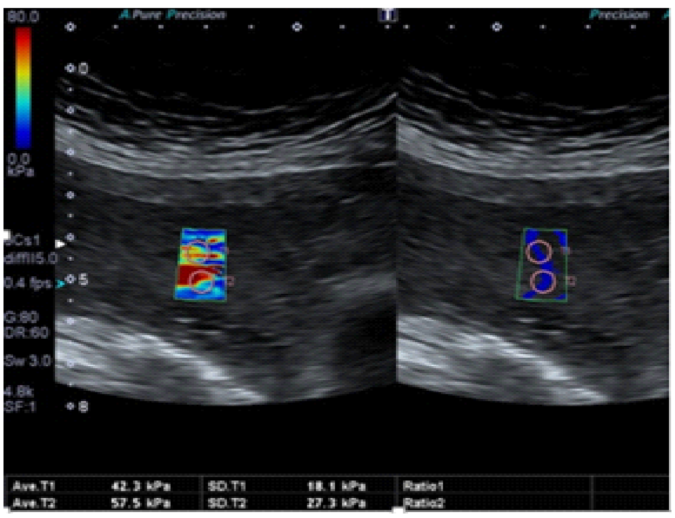


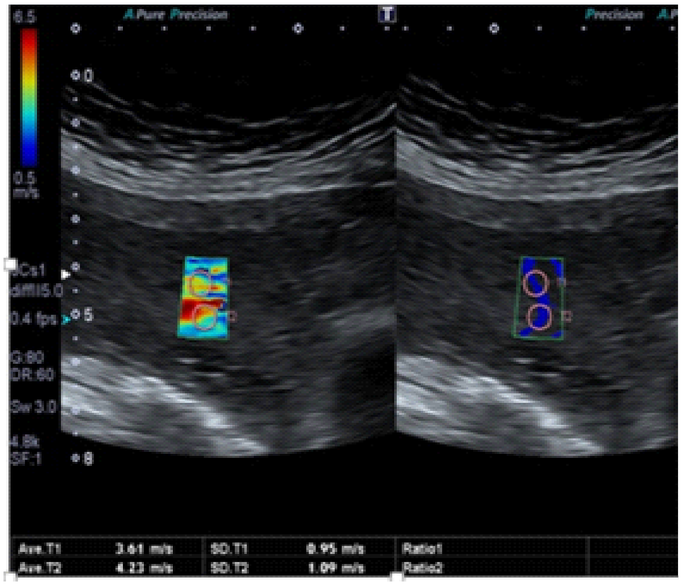
Case 1 hypotrophic fetus. Image (A, B) shows fetus at 32weeks of pregnancy. Biometry showed BPD corresponding to 32 weeks. Fetal weight below 10th percentile. FL is lagging 4 weeks behind BPD & AC lagging behind 3 weeks behind BPDsevere oligohydramnios 3.12cm.



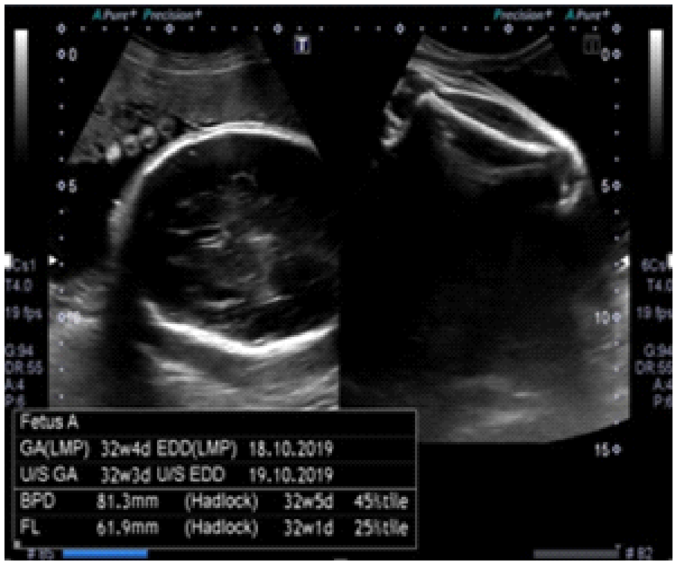


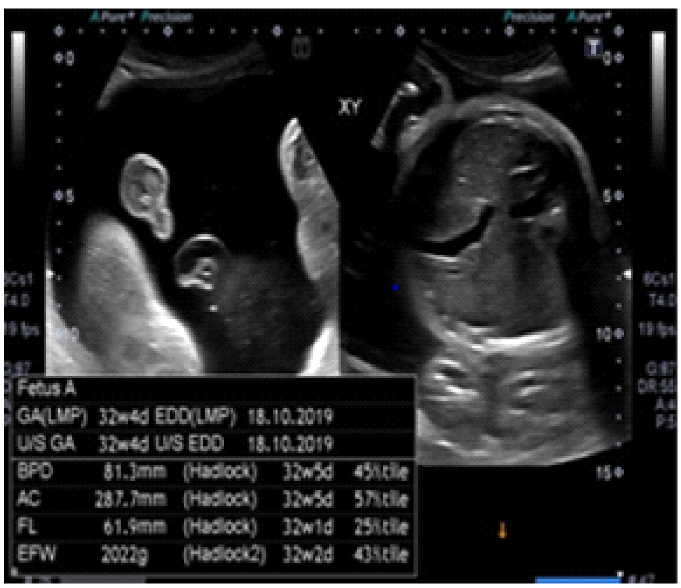
Case 1: Image (C,D,E) of the same fetus at 32 weeks showing uterine artery with persistent post systolic notch , having S.D 3.72 and R.I 0.73 high resistant flow.In Image D umbilical artery showing reversal flow with S.D 4.52 and R.I 1.22 indicative of fetal distress. Image E is of middle cerebral artery which shows S.D 2.55&R.I 0.61 with brain sparing phenomenon.

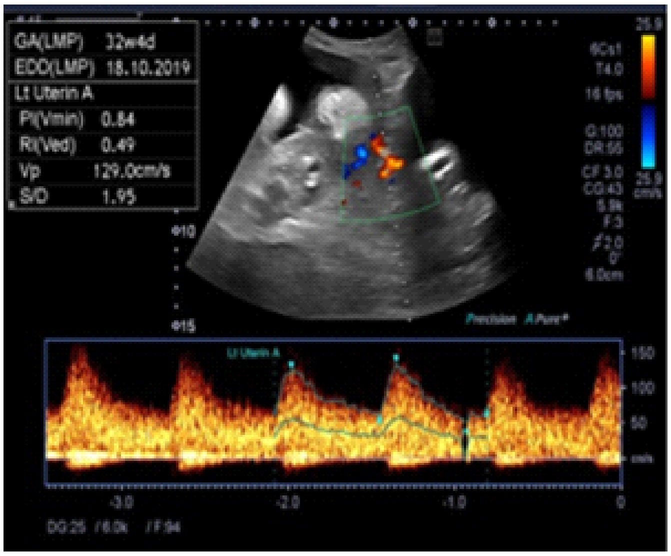




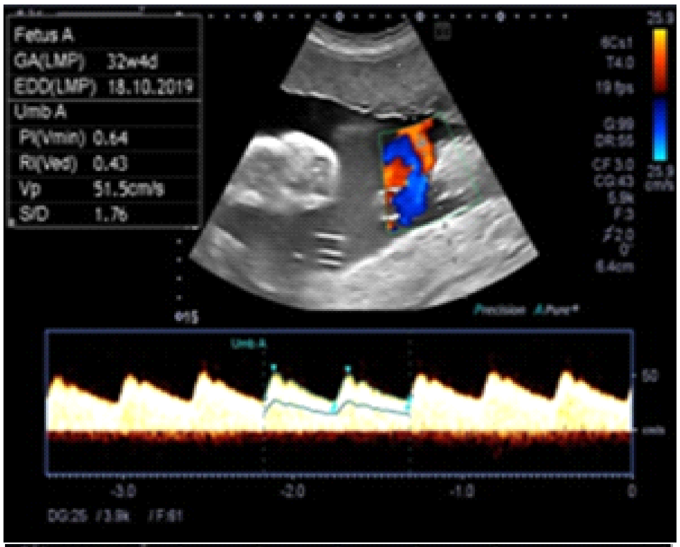
Case1: Image F is showing a high mean placental elasticity value 49kpa

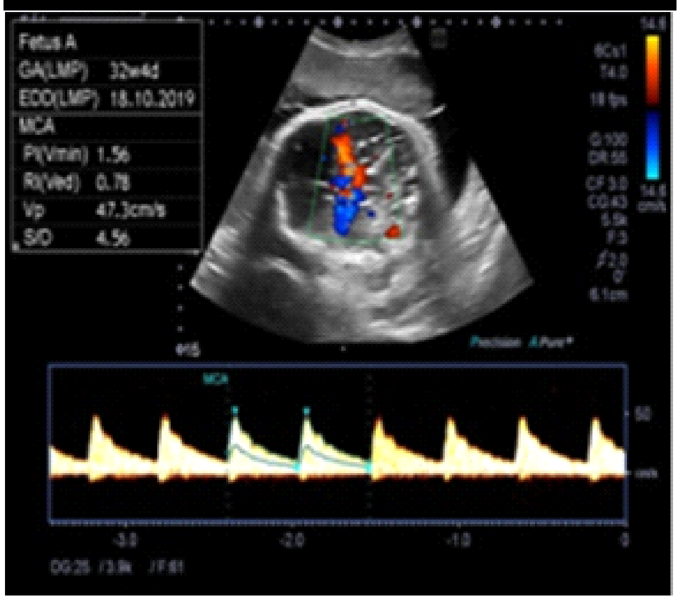


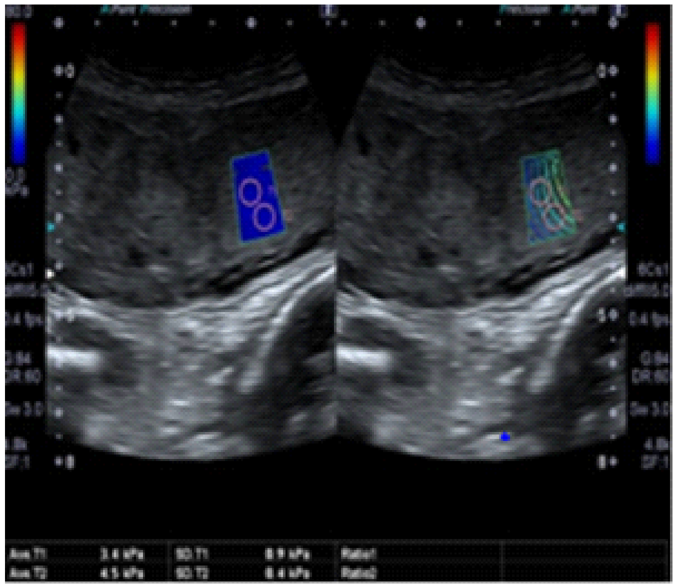




Case 2 normal fetus: Images A, B showing normal biometric values at 32 weeks. Image C, showing normal forward diastolic flow in uterine artery.







Case2: Image D, E, F Image D showing normal forward diastolic flow & umbilical artery with R.I 0.43 Image E showing MCA with high resistant flow with R.I 0.78 Image F showing normal low placental elasticity i.e 3.4kpa

Conclusion:

We established the diagnostic application of SWE imaging in IUGR, because conventionally IUGR is detected by fetal biometry on Doppler indices, which is very hectic and usually early detection is missed. But with this placental shear wave elastography, diagnosis is with single step, easy to operate, low cost, immediate report and possibility of early management. Therefore, we strongly recommend that as a new technique of tissue categorization shear wave elastography is worthwhile for assessment of placental dysfunction.

Ethical Approval: Given
Conflict of Interest: The authors declare no conflict of interest.
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