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Comparative evaluation of placental elasticity in normal pregnancy and pregnancy-induced hypertension and its association with uterine artery pulsatility index and fetal outcome

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ABSTRACT

Background: Pregnancy-induced hypertension (PIH) is associated with significant maternal as well as fetal morbidity and untreated cases may be associated with poor pregnancy outcomes. It brings about various histological and morphological changes in the placenta such as infarcts, fibrosis, and calcification thereby affecting the well-being of fetus. Detection of it at an early stage is important from the point of view of management as early intervention is associated with improved maternal and fetal outcome. Shear wave elastography (SWE) of placenta is a non-invasive investigation that can detect changes in placental elasticity during the pregnancy. **Aims and Objectives:** The aim of the study was to assess and compare the difference in values of placental elasticity in normal pregnancy and in clinically diagnosed cases of PIH and to study its association with uterine artery-pulsatility index (UtA-PI) and fetal outcome. **Materials and Methods:** This was a prospective and observational study in which pregnant females with gestational age of 20–34 weeks who were referred to radiology department for routine sonography including the clinically diagnosed pregnancies with PIH were included on the basis of a predefined inclusion and exclusion criteria. A total of 106 individuals were included in the study, B-mode sonography, uterine artery Doppler, and placental SWE were performed in all these patients. All these pregnancies were followed up for the fetal outcome. **Results:** The mean gestational age of the studied cases was found to be 26.51 ± 4.415 weeks. Higher SWE values were found, as compared to the normal pregnancies, in pregnancies complicated by PIH and the difference was found to be statistically highly significant ($P < 0.001$). Placental SWE showed a strong association with UtA-PI and fetal outcome. Incidence of adverse fetal outcome such as preterm deliveries, intrauterine death, stillbirths, and small for gestational age babies was more commonly seen in PIH group and the difference was statistically significant ($P < 0.005$). Incidence of birth asphyxia (as determined by low APGAR score) and neonatal intensive care unit admissions was more in neonates born to patients with PIH as compared to those in healthy women and the difference was statistically significant ($P < 0.005$). **Conclusion:** SWE has the potency to detect the changes in placental morphology and can help with diagnosis of pregnancies complicated with PIH. It does have a synergistic role to play alongside the uterine artery Doppler and clinical parameters to predict the pregnancies with PIH.

Key words: Doppler; Elastography; Fetal outcome; Pregnancy induced hypertension

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INTRODUCTION

Fetus derives its nutrition from the placenta which acts as a vital organ for normal growth and development of fetus. Structurally, placenta is appropriately adapted to achieve this by having a large surface area and a thin membranous connection in between the maternal and fetal circulation to allow for gaseous and nutrients exchanges.

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Placenta brings about the changes in the maternal uterine arteries and remodel them in a way that is efficient to facilitate these physiological transfer/exchange, when these changes do not take place as they should, then there arise the complications in pregnancy and pregnancy-induced hypertension (PIH) is one such result of poor invasion of maternal uterine spiral arteries by the trophoblast cells.[1] The hypertensive disorders manifest as a direct result of gravid state for the first time in pregnancy after 20 weeks, they are termed as pregnancy-induced hypertensive disorders.[2] Complications during pregnancies, result in maternal and/or perinatal mortality as well as significant morbidity. Hence, a detailed evaluation of placenta during the routine antenatal scan is of great importance to predict the associated complications. Early diagnosis of PIH as well as Doppler abnormalities in these cases can be helpful in alerting the treating gynecologists and consequently appropriate treatment can be started at the earliest so that incidence of complications such as preterm delivery, intrauterine fetal demise, and small for gestational age (SGA) babies can be prevented or at least reduced.[3]

Since the uteroplacental perfusion is inadequate in pregnancies complicated with PIH, use of Doppler sonography to assess the uterine artery blood flow may be a marker of severity of PIH.[4] The Doppler findings which may be present in patients with uncontrolled PIH and have a predictive value include presence of bilateral uterine artery notching and increased Pulsatality index.[5] Another imaging technique which can be used for assessing severity of PIH includes shear wave elastography (SWE). It is a novel ultrasonography (USG) technique which has been used for benign and malignant lesions of breast, thyroid, prostate, kidney, spleen, and lymph node characterization. It can also be used for diagnosis of hepatic abnormalities such as fibrosis and cirrhosis of liver.[6] SWE generates the short acoustic pushing pulse that causes the displacement in the target tissue which when recoils back and gives a measurable velocity.[7] The technique is used to know about the soft-tissue constituent by determining its elasticity.[8]

As the stiffness of any tissue increases, there is proportional increase in shear wave elasticity and SWE can be reliably used to predict the possibility of development of PIH and cases with increased SWE then can be kept under strict follow-up. Placenta being a soft tissue, this technique can be considered to study the changes in its histology. SWE is found to be safe and has no detrimental effect on fetal health.[9] Lately in recent years, few studies had come up with their results to depict the role of SWE in assessment of placental elasticity but presently there are limited data available in Indian population and further studies are required to further substantiate the findings of studies done on the subject.

With this background, this study had been undertaken to evaluate placental elasticity changes in pregnancies with PIH and to determine its correlation with the uterine artery-pulsatality index (UtA-PI) and fetal outcome.

Aims and objectives

The objectives of the study are as follows:
(1) To assess and compare the difference in values of placental elasticity in normal pregnancy and in clinically diagnosed cases of PIH. (2) To study association of placental elasticity with UtA-PI and fetal outcome.

MATERIALS AND METHODS

This was a prospective and observational study conducted in the Department of Radiodiagnosis, Teerthanker Mahaveer Medical College and Research Centre, Moradabad. One hundred and six pregnant females referred for imaging and having gestational age of 20–34 weeks were included in this study on the basis of a predefined inclusion and exclusion criteria. The study was approved by our Institutional Ethical Committee. Written and informed consent was obtained from all the subjects. Pregnancies with multiple gestations, major congenital structural anomalies, history of smoking, any pre-existing comorbidities, systemic obstetric disorders other than PIH, and the placenta with the depth exceeding 10 cm (which precludes elastography) were excluded from the study. The patients were divided into two groups.

- Group A: 77 women with normal pregnancies of gestational age between 20 and 34 weeks not complicated by PIH.
- Group B: 29 women with pregnancies of gestational age between 20 and 34 weeks and had a clinical diagnosis of PIH.

The clinical data and laboratory investigations (if available) were documented. All pregnant women were evaluated on USG machine Acuson S3000 (SIEMENS, Germany)/USG machine SIEMENS Acuson Juniper VA10F. B-mode USG, Doppler study, and placental elastography were performed in a single sitting.

B-mode USG was done using curvilinear transducer (5C1/6C1). The gestational age of the fetus was determined and the placenta was localized, pregnancies with placenta at >10 cm depth were excluded from the study. Uterine artery Doppler was done using the same curvilinear transducer, color Doppler of bilateral uterine arteries was performed to assess the uteroplacental circulation. The spectral waveform was analyzed. Pulsatality index of the right and left uterine arteries was documented. Any diastolic notching, if present unilaterally/bilaterally was documented as well. The values of UtA-PI more than the 95th percentile for the

specific gestational age were considered abnormal. SWE of placenta was performed using curvilinear transducer (5C1/6C1) wherever feasible linear transducer (9L4) was used (when the depth of placenta was not more than 4cm).

The elasticity of the placenta was assessed using SWE, the examination required pregnant female to perform shallow breathing for 5 s. The SWE values were measured in the mid substance of placenta at the upper pole, lower pole, and center of the placenta (2 cm away from cord insertion). Three readings were taken at the three sites and mean was calculated.

Fetal outcome was evaluated using parameters such as incidence of adverse outcome such as preterm deliveries, intrauterine fetal demise, stillbirth, perinatal mortality, low birth weight, Birth asphyxia (as assessed by 1 min and 5-min APGAR scores), and the need for neonatal intensive care unit (NICU) admissions.

All these findings were documented and analyzed to evaluate the SWE values of placenta in normal pregnancies and in pregnancies complicated with PIH and the correlation of these with the UtA-PI values and fetal outcome was studied.

SSPS 21.0 version was used for statistical analysis and P<0.05 was taken as statistically significant.

RESULTS

Mean gestational age for pregnancies in Group A was around 25.61±4.248 weeks whereas mean gestational age of patients in Group B was 28.92±.981 weeks. The mean gestational age of the studied cases was found to be more in PIH group (Group B) as compared to non-PIH group (Group A) and the difference was found to be statistically significant (Table 1).

The placental location was determined by gray scale imaging. The most common type of placenta was anterior (42.45%) followed by posterior (21.70%) and fundoposterior (14.15%). Least common type of placenta was found to be posterolateral placenta which was seen in 2 (1.89%) patients. Placenta was homogenous in echotexture in 93 (87.74%) patients whereas in remaining 7 (12.26%) patients' placenta was heterogeneous in echotexture. The placenta was found to be heterogeneous predominantly in patients with PIH as compared to non-PIH group and the difference was found to be statistically significant (P<0.001) (Table 2).

Placental SWE values at three poles were analyzed, with mean values ranging from 1.95–2.10 kPa at upper pole, 2.08–2.18 kPa at mid pole, and 1.92–2.04 kPa at lower pole in Group A (non-PIH). An overall mean value of SWE was 2.03±0.471 kPa was seen in Group A (non-PIH). In Group B (PIH group), SWE showed mean values ranging from 6.36–6.82 kPa at upper pole, 7.30–7.76 kPa at mid pole, and 6.78–7.06 kPa at lower pole. An overall mean value of SWE was 6.98±1.229 kPa. Placental SWE values at three poles were significantly higher in Group B as compared to Group A (P<0.001) (Table 3 and Figure 1).

The analysis of uterine artery Doppler showed that mean PI was 0.95±0.388 in the right uterine artery and it was 0.90±0.319 in the left uterine artery whereas in Group B (PIH group) a mean PI of 1.91±0.522 in the right uterine artery and a mean PI of 1.81±0.421 in the left uterine artery was observed. Mean PI of PIH group was higher as compared to non-PIH group and the difference was found to be statistically significant. Diastolic notch was observed in uterine arteries of some of these patients either unilaterally or bilaterally (Table 4 and Figure 2).

The analysis of fetal outcome showed that incidence of preterm deliveries was more common in PIH Group as compared to non-PIH group and the difference was found to be statistically significant (P<0.001). There were 8 (7.55%) cases of intrauterine fetal demise (7.55%) and 4 cases (3.77%) of stillbirths in PIH group. There was no intrauterine death (IUD) or still birth in non-PIH group. The incidence of PIH and IUD was found to be more in PIH group and the difference was statistically significant (P<0.001). All neonates were appropriate for gestational age in non-PIH group whereas 18 (16.98%) patients were SGA in PIH group. The difference was statistically significant (P<0.001). No neonate in non-PIH group required admission in NICU whereas 13 (12.26%) neonates from PIH group had to be admitted in NICU for various reasons. The need for NICU admission was high in PIH group as compared to non-PIH group and the difference was statistically significant (P<0.005) (Table 5).

Finally, APGAR scores at 1 min and 5 min were analyzed in neonates in both the groups. The mean APGAR score

Table 1: Comparison of mean gestational age in studied cases

Mean gestational age on USG	Non-PIH (Group A)			PIH (Group B)			P value
	Mean±SD	Min–Max	Median (Q1–Q3)	Mean±SD	Min–Max	Median (Q1–Q3)	
In weeks	25.61±4.248	20–34	24.71 (21.71–29.65)	28.92±3.981	21–34	30.71 (25.08–32.29)	0.001
In days	179.23±29.732	141–237	173 (152–207.5)	202.45±27.872	144–235	215 (175.5–226)	0.001

SD: Standard deviation, PIH: Pregnancy induced hypertension, USG: Ultrasonography

Table 2: Comparison of placental location and placental echotexture in studied cases

Placental Location and Echotexture	Non PIH (Group A)		PIH (Group B)		P value
	Frequency	%	Frequency	%	
Placental location					
Anterior	35	33.02	10	9.43	<0.001 (Significant)
Antero-lateral	3	2.83	2	1.89	
Fundal	2	1.89	3	2.83	
Fundo-anterior	2	1.89	2	1.89	
Fundo-posterior	10	9.43	5	4.72	
Lateral	5	4.72	2	1.89	
Posterior	20	18.87	3	2.83	
Posterolateral	0	0.00	2	1.89	
Total	77	72.64	29	27.36	
Placental echotexture					
Heterogeneous	1	0.94	12	11.32	<0.001 (Significant)
Homogeneous	76	71.70	17	16.04	
Total	77	72.64	29	27.36	

PIH: Pregnancy-induced hypertension

Table 3: Comparison of shear wave elastography in studied cases

Placental elastography	Non PIH (Group A)			PIH (Group B)			P value
	Mean±SD	Min–Max	Median (Q1–Q3)	Mean±SD	Min–Max	Median (Q1–Q3)	
Upper pole							
1st	1.95±0.743	0.8–3.64	1.82 (1.28–2.55)	6.36±1.842	3.6–11.2	5.83 (4.855–7.725)	<0.001
2nd	2.1±0.777	0.9–4.68	1.98 (1.46–2.76)	6.82±2.03	2.94–11.6	6.88 (5.145–8.16)	<0.001
3rd	2.06±0.678	0.95–4.32	1.98 (1.56–2.35)	6.55±1.828	3.3–12.1	6.66 (5.32–7.195)	<0.001
Midpole							
1st	2.08±0.916	0.76–4.1	1.98 (1.25–2.56)	7.3±2.279	3.93–13.7	7.01 (6–8.16)	<0.001
2nd	2.09±0.843	0.8–4.32	2.04 (1.34–2.635)	7.68±2.072	3.98–12.7	7.84 (6.235–8.805)	<0.001
3rd	2.18±0.765	0.9–4.9	2.04 (1.63–2.79)	7.76±2.131	3.7–13.6	8.12 (6.605–9.12)	<0.001
Lower pole							
1st	1.94±0.776	0.9–4.24	1.88 (1.32–2.43)	7.06±2.459	3.6–13.9	6.9 (5.41–7.98)	<0.001
2nd	2.04±0.728	0.89–4.43	1.98 (1.38–2.59)	6.99±2.045	3.84–11.2	6.87 (5.07–7.995)	<0.001
3rd	1.92±0.673	0.8–3.88	1.88 (1.42–2.295)	6.78±1.979	3.2–10.9	6.24 (5.545–8.64)	<0.001
Mean SWE values	2.03±0.471	1.1–3.22	2 (1.66–2.335)	6.98±1.229	4.59–9.71	6.94 (5.985–7.97)	<0.001

PIH: Pregnancy-induced hypertension, SWE: Shear wave elastography, SD: Standard deviation

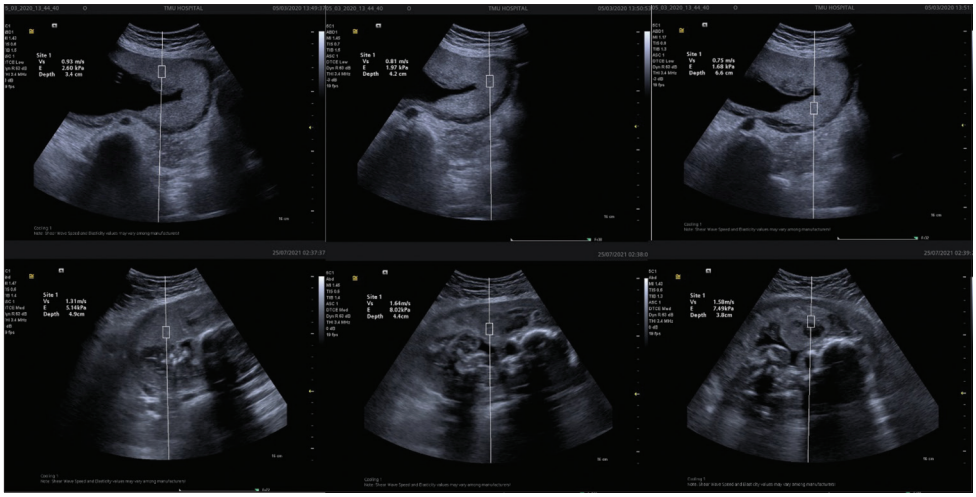

Figure 1: Comparison of placental shear wave elastography values and echotexture of healthy pregnant women (upper row) and pregnancies complicated with pregnancy-induced hypertension (bottom row)

at 1 min in non-PIH and PIH group was found to be 9.21±0.675 and 6.0±0.707, respectively, whereas at 5 min, it was 9.70±0.46 and 7.76±0.83. The APGAR scores at 1 min and 5 min were found to be higher in non-PIH group as compared to PIH group and the difference was found to be statistically significant (P<0.001) (Table 6).

Table 4: Comparison of uterine artery Doppler parameters in studied cases

Uterine artery PI	Non PIH (Group A)			PIH (Group B)			P value
	Mean±SD	Min–Max	Median (Q1-Q3)	Mean±SD	Min–Max	Median (Q1-Q3)	
RUA	0.95±0.388	0.45–2.69	0.86 (0.69-1.015)	1.91±0.522	1.14–3.4	1.89 (1.53-2.11)	<0.001
LUA	0.9±0.319	0.43–1.9	0.84 (0.675-1.015)	1.81±0.421	1.03–3.15	1.87 (1.66-1.97)	<0.001

PIH: Pregnancy induced hypertension, PI: Pulsatility index

Table 5: Comparison of neonatal outcome in studied cases

Term/preterm	Non PIH (Group A)		PIH (Group B)		P value
	Frequency	%	Frequency	%	
Term/preterm delivery					
Preterm	0	0.00	23	21.70	<0.001
Term	77	72.64	6	5.66	
Total	77	72.64	29	27.36	
Fetal outcome					
IUD	0	0.00	8	7.55	<0.001
Live	77	72.64	17	16.04	
Stillbirth	0	0.00	4	3.77	
Total	77	72.64	29	27.36	
Weight					
AGA	77	72.64	11	10.38	<0.001
SGA	0	0.00	18	16.98	
Total	77	72.64	29	27.36	
Need for NICU admission					
Yes	0	0.00	13	12.26	<0.001
No	77	72.64	16	15.09	
Total	77	72.64	29	27.36	

PIH: Pregnancy-induced hypertension, IUD: Intrauterine death, AGA: Appropriate for gestational age, SGA: Small for gestational age, NICU: Neonatal intensive care unit

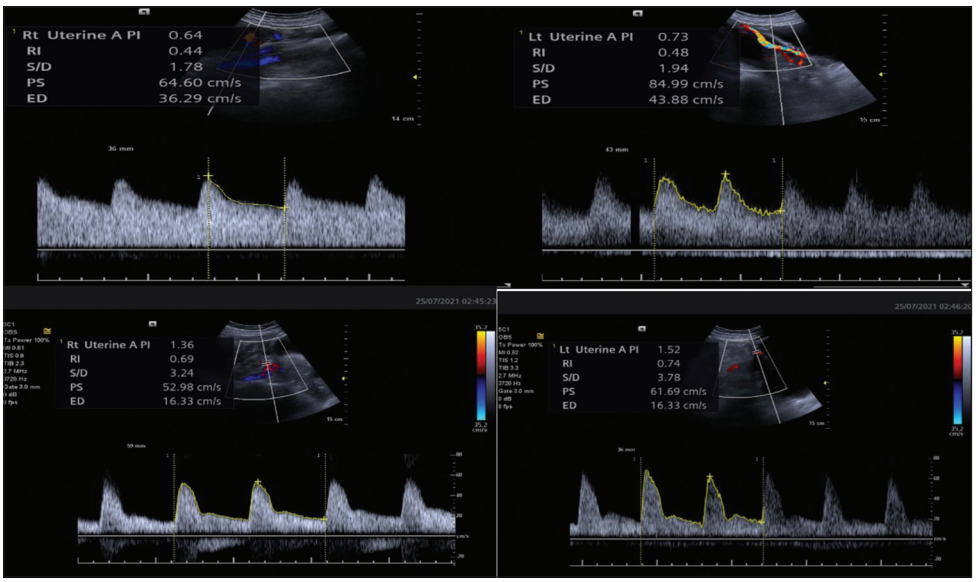

Figure 2: The uterine artery Doppler in the same pregnant females presented in Figure 1. Doppler indices in healthy pregnant women (top row). High uterine artery-pulsatility index values along with early diastolic notching were observed in pregnancy complicated with pregnancy-induced hypertension (bottom row) which showed abnormal shear wave elastography values as presented in Figure 1

On plotting a receiver operating characteristic curve using fatal-fetal outcome and the SWE as variables, the area under the curve was 0.52 which was not significant, it was observed that although the SWE of placenta was able to predict the poor fetal prognosis but it could not determine the severity of the fetal outcome (Figure 3).

DISCUSSION

SWE is a non-invasive and quantitative technique to study tissue morphology and pathological changes in them by evaluating tissue elasticity.[10] It has been gaining importance in evaluation of elasticity of various organs such as liver,

Table 6: Comparison of APGAR scores in neonates in studied cases

APGAR score	Non PIH (Group A)			PIH (Group B)			P value
	Mean±SD	Min–Max	Median (Q1-Q3)	Mean±SD	Min–Max	Median (Q1-Q3)	
At 1 min	9.21±0.675	8–10	9 (9–10)	6.0±0.707	5–7	6.0 (5.5–6.5)	<0.001
At 5 min	9.70±0.46	9–10	10 (9–10)	7.76±0.83	6–9	8 (7–8)	<0.001

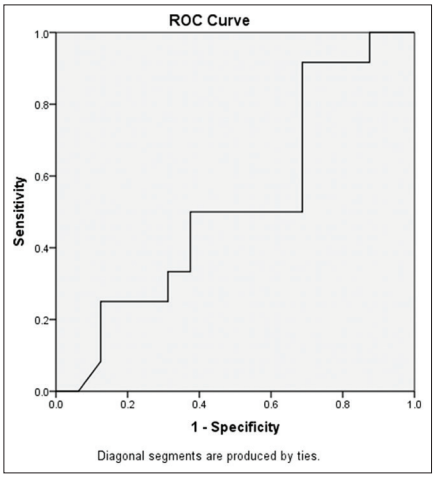

Figure 3: Receiver operating characteristic curve for shear wave velocity and fetal outcome

prostate, thyroid, spleen, and cervix. In recent years, various studies had been conducted which established the role of SWE to study the placental morphology and histological changes that occur in the pregnancy.[11]

Dokumaci and Uyanikoglu conducted the study in which the authors differentiated normally localized placenta and placenta previa on the basis of SWE of placenta.[12] Sugitani et al., conducted an *ex-vivo* assessment of placental elasticity and correlated with the histological changes observed in the placentas.[13] Simon et al., reported their SWE findings in the normal pregnancies and pre-eclamptic pregnancies.[14] It was noted that not much data were available in Indian population assessing the predictive value of the placental elastography and its association with the UtA-PI and fetal outcome. Our results suggested that placental SWE values were significantly higher in the pregnancies complicated with PIH as compared to the normal pregnancies.

In our study, for normal pregnancy group subjects, the mean values were 2.03±0.471kPa and for PIH group subjects, the mean values were 6.98±1.229 kPa. Altunkeser et al., in his study reported that the SWV values were higher at the central region of placenta as compared to the periphery which was observed in our study as well, since the SWE elasticity values were higher at the mid pole.[15] In our study, overall mean placental elasticity values were found to be higher in pregnancies complicated with PIH as compared to the normal pregnancies.

In a study conducted by Kiliç et al., placental shear modulus values were higher for pregnancies with pre-eclampsia with a mean of 7.35 kPa having 90% sensitivity and a specificity of 86% and the study also concluded that the values were higher at the center of placenta. The study also presented a correlation with uterine artery Doppler indices.[16]

A study conducted by Cimcit et al., reported that shear wave elastographic values for PIH group were significantly higher than those for normal group ($P<0.05$).[17] Another study conducted by Ohmaru et al., also reported higher Shear wave velocities in placentas of pregnancies with pre-eclampsia and intrauterine growth restriction.[18] Fujita described the SWV in low-risk and high-risk pre-eclampsia groups among the women of gestational age 20–32 weeks and reported that values were higher in high-risk groups with values ranging from 0.64–1.47 m/s in low-risk PE groups and 0.76–2.39 m/s in high-risk PE groups.[19] The results from our study resonated with the results from the mentioned studies.

SWE has an advantage, that is, it does not require any additional device and can be performed in the same visit when the antenatal scan is done. It is a non-invasive technique with no harmful mechanical or thermal effects on maternal or fetal well-being. Hence, the safety of the technique is not questionable. The acoustic radiation force impulses are generated and there is no compression required; hence, it is operator independent. It was observed that placing the region of interest required the operator focus, it was placed away from any lacunae, vessels, or calcification focus to avoid discrepancies in the measurements. This practice was also documented in a study by Li et al.[20] Overall, it can be summed up that SWE of placenta can be considered for the evaluation of the placenta along with the previous mentioned techniques.

Uterine artery Doppler in our study revealed abnormal values of uterine artery PI or diastolic notching in PIH group either unilateral or bilateral. These findings in our study were consistent with a study conducted by Karaman et al., which reported that the Doppler findings showed presence of diastolic notch in bilateral uterine arteries in PIH patients with significantly high Pulsatality index values.[21] Another study done by Gomez et al., suggested that mean uterine artery PI may have clinical relevance in screening for placenta associated diseases in the early stages of pregnancy and in evaluation of patients with PIH during the late trimester.[22]

The uterine artery Doppler findings were coinciding with the higher SWE values that were found in PIH group.

The pulsatality index of the uterine arteries was higher in pregnancy-induced hypertension individuals. According to a study conducted by Raman et al., the uterine arteries' mean pulsatality index is a good screening indicator for the risk of pregnancy-induced hypertension.[23] With increasing gestational age, the uterine artery pulsatality index begins to decrease. After 21 weeks of pregnancy, it is never >1.54. The uterine artery wave shape does not have any notches in the diastolic flow.

Out of total subjects under normal pregnancy group, all completed their full term whereas in case of PIH group, only 6 (20.6%) subjects completed their term whereas rest of them had perinatal complications including preterm delivery, IUD, stillbirth, and even maternal mortality. These findings were consistent with the studies conducted by Unnisa[24] and Mulualem et al.,[25] who reported that the group with pre-eclampsia had more perinatal complications as compared to healthy pregnant women without PIH. It was observed in our study that the abnormal placental SWE values were associated with a poor fetal outcome but it could not predict the severity of poor perinatal outcome.

Limitations of the study

Technical limitation of being able to include only those patients who had placenta at a depth of <10 cm and relatively small number of patients were the limitation of our study. A large comparative study will further substantiate the findings of our study.

CONCLUSION

Imaging aided by SWE of the placenta when performed during pregnancy can help in predicting risk of maternal and perinatal complications. SWE can be used as a tool for evaluation of placental function and as a supplement to the existing methods for prediction of PIH.

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AC- Concept and design of the study, interpreted the results, prepared first draft of manuscript, and critical revision of the manuscript; **SP-** Statistically analyzed and interpreted, reviewed the literature, and manuscript preparation; **AM-** Design of the study, statistically analyzed and interpreted, preparation of manuscript, and revision of the manuscript; and **SA-** Concept and coordination of the overall study.

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