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ORIGINAL ARTICLE

Strain Cervical Elastography in Pregnancy: Feasibility Study and Its Usefulness in Prediction of Preterm Birth

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Abstract Cervix in pregnancy is a biomechanical barrier holding the uterine contents till the time of parturition. The feasibility and reproducibility of assessing cervical tissue stiffness for predicting preterm birth by a standard method using strain cervical elastography were studied here. The prospective study included use of transvaginal strain elastography assessment of cervix at 22–24 weeks in three regions of interest: (1) Endocervical canal and entire cervix in mid-sagittal plane (2) At the level of external os in cross section and (3) at the level of internal os in cross-sectional plane, with constant pressure application each time. Strain ratios were recorded twice for the operator 1 and once by operator 2. Cervical length was also measured according to standard protocol. The measurement of strain ratios was possible in all the 85 included cases. Intra or and inter operator agreement was good for all the 3 ROIs by Kappa analysis and Pearson coefficient. In 10 cases of preterm birth with cervical length ≤ 25 mm, the strain ratios at internal os were observed to be < 1. Strain cervical elastography in pregnancy appears to be a novel, feasible and reproducible technique using a standard method for prediction of preterm birth.

Keywords Cervical elastography · Strain elastography · Preterm birth · Cervical stiffness

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Introduction

Pregnant uterus is like a balloon and the cervix is its mouth. As long as the cervix is closed, firm and long, the contents of the uterus remain safe inside. The cervix undergoes series of changes during pregnancy known as cervical remodeling. Changes like softening/ripening, dilatation and shortening help in parturition [1, 2]. Premature occurrence of these changes can result in preterm birth or cervical incompetence leading to miscarriage. Conventionally, digital examination or sonological cervical length assessment are used for prediction of these events [3]. However, the untouched property-"stiffness" has now been exploited in prediction of preterm birth by the novel technique of elastography. Elastography is a sonological tool used to study elasticity or stiffness of the tissue of interest. Initially used as a qualitative assessment, quantitative assessment by strain elastography (static) and shear wave elastography (dynamic) has now been applied in obstetrics [4, 5]. The study presented here evaluated and attempted to develop a standard and scientific method of assessment which could be clinically used. The objectives of the study were: (1) To formulate a standard technique of strain elastography for cervix in pregnancy and to study its feasibility (2) To study its reproducibility by assessing the intra observer and inter observer correlation and (3) To examine its usefulness in prediction of preterm birth in association with the conventional measurement of cervical length.

Materials and Method

This was a prospective study that included 85 consecutive unselected singleton pregnancies with gestation age of 22–24 weeks. The study was carried out using

transvaginal endocavitory probe (IC 5-9, 8–4 MHz, LOGIQ E9, GE Healthcare, Milwaukee, WI). Those women who were on progesterone or had previous history of preterm delivery/spontaneous mid trimester miscarriage or had a history of cervical encerclage or cervical surgery were excluded from the study. All the patients included were provided information leaflet regarding the study and written consent for the same was obtained. Cervical length was transvaginally measured with the patient in dorsal position (with empty bladder) for all included patients using the standard technique [3] in midsagittal plane avoiding any compression by the probe. This was followed by elastography evaluation in following three regions of interest (ROI) for strain calculation (Figs. 1 and 2): (1) Endocervical canal and entire cervix in mid-sagittal plane (2) At the level of external os in cross section and (3) at the level of internal os in cross-sectional plane. In each plane a reference point was chosen in the blue region on elastograph (suggesting stiffest area) outside the cervix (just posterior or lateral to the cervix over the ligament insertion, avoiding any fluid area). After interrogating each region of interest using the elastography colour box in a paired image, continuous oscillatory pressure (stress) by the ultrasound probe was applied for 3 s. The pressure was controlled and quantified by the pressure indicator bar displayed on top left of the monitor screen. This was repeated again by the same observer and then by the second observer. Strain ratios were calculated by the performing observer in all the three regions of interest. Operators were not aware of the measurements of each other and the first observer calculated the strain ratios only after both her observations were saved as a cine loop. The measured strain values represented the percentage of displacement or deformation of tissues within the cervical area averaged among consecutive ultrasound frames during manual application of oscillatory pressure.

The rationale of selecting three regions was that in the midsagittal section, cervical length can be measured along with calculation of the average strain in the endocervical canal and the whole cervix. The cross section at the two levels are selected to assess and compare the tissue strains in well defined regions of the cervix and where the earliest changes are expected to occur in patients of threatened preterm labour. The gestation age of 22–24 weeks was chosen as it is an ideal age of screening for preterm birth and risk calculation [3].

Statistical Analysis

Inter operator agreement for tissue-strain was assessed using the Cohen kappa statistic. Additionally, the Pearson correlation coefficient was calculated to assess intra and inter operator correlation. Statistical analyses were performed with SPSS 18.0 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

Strain elastography measurement was possible in all 85 pregnancies (100%). Three sets of strain ratios (two sets for observer 1 and one set for observer 2), each set consisting of 595 (85 × 7) strain ratios were obtained and noted. All the 1785 strain values were recorded and analyzed. Maternal characteristics of the study population are depicted in Table 1. Kappa analysis of the strain ratios showed a significant correlation between two sets of strain ratios obtained by the same observer and also between the respective sets of strain ratios of Observer 1 and 2. This was re-emphasized by Pearson coefficient using 95% confidence interval (Table 2). In 10 cases of preterm birth with cervical length ≤ 25 mm, the strain ratios at internals

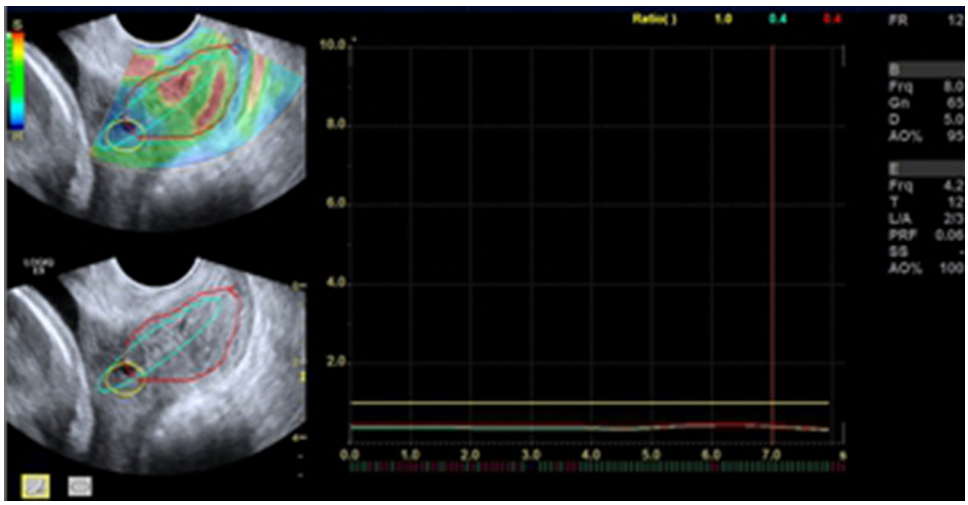

Fig. 1 Strain elastography assessment in mid sagittal view

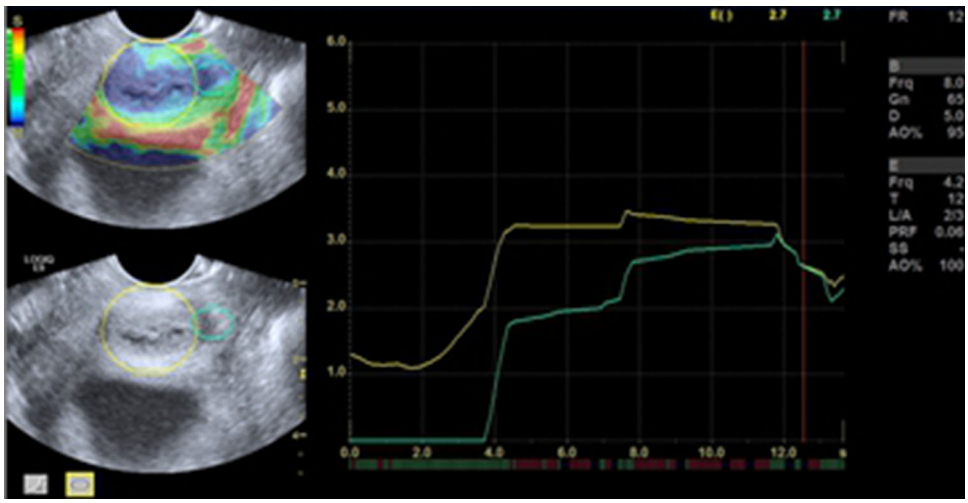

Fig. 2 strain elastography assessment in cross section at the level of internal os

Table 1 Maternal characteristics of the study population

Age (mean)	28.5 years
Ethnicity	South Asian (Indian)
Parity (mean ± SD)	1.5 ± 0.65
Cervical length (mean ± SD)	29.33 mm ± 4.88 mm
Gestational age (mean ± SD)	22.5 weeks ± 1.90 weeks

were observed to be < 1. On an average the strain ratios of the endocervical canal in those delivering at term were higher than that of the whole cervix.

Discussion

Prediction of preterm birth has been a major area of current interest and newer laboratory and sonological methods are studied. Elastography as a tool of measuring cervical tissue stiffness has gained attention in the last decade and its application in prediction of preterm birth, in prediction of induction to delivery interval as well as gynecological diseases has been evaluated [4, 5].

Our study signified that cervical strain elastography by the method described above is reproducible and feasible. Since there was no failure of strain measurement in any of the women, the method used is operator friendly and feasible. The Kappa analysis and Pearson coefficient showed good intra operator and inter operator correlation and thereby signified the method to be reproducible. Elastography is based on the principle that elasticity = stress/strain, where stress is the pressure applied per unit area, strain is the tissue deformation in response to strain and elasticity is the stiffness or resistance of the tissue to deformation. Strain ratio is the difference between the displacement of the ROI and that of the reference point [4, 5]. Based on the above principles, it is imperative that stress or pressure applied by the transducer is constant or uniform for each case. This was controlled with the help of pressure indicator bar that proportionally reflected the

Table 2 Kappa analysis and Pearson coefficient for intra operator and inter operator correlation

	Simple kappa	95% CI	Weighted kappa	95% CI	Pearson's coefficient
(A) Intra observer correlation					
Endocervix	0.089	0.000241 to 0.178	0.558	0.139–0.667	0.40
Entire cervix	0.117	0.00842 to 0.225	0.453	0.289–0.616	0.44
Internal os	0.113	0.006 to 0.219	0.414	0.231–0.596	0.67
External os	0.283	0.156 to 0.411	0.549	0.404–0.694	0.71
(B) Inter observer correlation					
Endocervix	0.0448	− 0.0315 to 0.121	0.535	0.391–0.678	0.68
Entire cervix	0.122	0.014 to 0.23	0.549	0.404–0.693	0.65
Internal os	0.0746	− 0.0228 to 0.172	0.414	0.245–0.583	0.68
External os	0.0505	− 0.034 to 0.136	0.522	0.376–0.667	0.76

stress in the study presented. The reference point in each was chosen in the region just outside the cervix as these tissues are known to be stiffer than the cervix in all circumstances by virtue of their composition. Unlike the use of normal tissue as a reference point which is done while using elastography for detecting malignancy, the reference point in case of cervical elastography cannot be within the cervix as the physiological changes during pregnancy occur in the entire cervix. Probe cap with known stiffness has been used in one study as a reference point, but practical use seems uncomfortable and incurs an additional cost [7]. Since the tissues just outside the cervix (ligaments) do not usually undergo major changes in their composition during pregnancy, they promise constant stiffness and good reference point for comparison.

Feasibility of quantitative cervical elastography in pregnancy has been studied in recent years using different methods [6–8]. Molina et al. [8] used a fixed circle of 6 cm for region of interest and the deformation of 1 cm and pioneered the use of cervical elastography. Andrade et al. [9] selected midsagittal and cross sections at the internal and external os and reported a fair reproducibility of cervical tissue strain with good correlation to cervical length but not with the gestational age. A common standardized method and approach is yet to be finalized. Our study also attempted to standardize the technique of strain cervical elastography in pregnancy by using above described methodology.

The strain ratio at internal os was < 1 in those delivering preterm. This finding can be supported by the pathophysiological changes taking place in cervix in preterm birth, wherein internal os becomes softer prior to the external os. Similar findings were also observed by Wozniak et al. [10]. The internal os cannot be assessed manually by digital examination but elastography promises its timely assessment for prediction of preterm labour. On an average, the strain ratios of the endocervical canal in those delivering at term were higher than that of the whole cervix and this can be explained by difference in the stiffness of the two regions [2, 4].

To our knowledge, no Indian study for cervical elastography in pregnancy has been carried out and our study is the first of its kind. Our study attempted to formulate a standard methodology for strain cervical elastography in pregnancy based on scientific approach and limiting the variables like stress and reference points to the best. Despite of these strengths, there are limitations like small sample size and drawbacks of strain elastography itself.

Conclusion

Strain cervical elastography in pregnancy appears to be a novel, feasible and reproducible technique using a standard method for prediction of preterm birth.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval Approved by Ethics committee, Indraprastha Apollo hospital.

Informed Consent Patient consents taken after information.

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