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Longitudinal Changes in Fetal Lung Elasticity Between 28–32 and 35–38 Weeks of Gestation in Healthy Singleton Pregnancies: A Prospective Observational Study

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Abstract

Background

This study aimed to evaluate longitudinal changes in fetal lung elasticity between the late second/early third trimester and late third trimester in healthy singleton pregnancies.

Methods

This prospective longitudinal observational study was conducted at a tertiary center between January and June 2025. Healthy singleton pregnancies without major fetal anomalies or obstetric/systemic conditions affecting fetal lung development were consecutively enrolled. Each participant underwent fetal lung 2D-SWE at two time points: 28–32 weeks and 35–38 weeks of gestation. Measurements were obtained using a standardized protocol, and fetal lung stiffness was recorded as Young's modulus (kPa) and shear wave velocity (m/s).

Results

Mean fetal lung stiffness decreased significantly from 2.65 ± 0.41 kPa at 28–32 weeks to 2.09 ± 0.43 kPa at 35–38 weeks ($p < 0.001$). Similarly, mean shear wave velocity decreased from 0.91 ± 0.07 m/s to 0.82 ± 0.08 m/s ($p < 0.001$). The observed reduction in elastographic values with advancing gestation suggests a progressive biomechanical change in the developing fetal lung. No preterm births or neonatal respiratory distress syndrome were observed in the study cohort.

Conclusions

In healthy singleton pregnancies, fetal lung elasticity decreases significantly between 28–32 and 35–38 weeks of gestation. These findings suggest that 2D-SWE may provide a feasible and noninvasive quantitative approach for characterizing longitudinal biomechanical maturation of the fetal lung. Larger multicenter studies, including high-risk pregnancies and neonatal respiratory outcomes, are needed to define the clinical utility of fetal lung elastography.

Introduction

Fetal lung development is a multilayered biological maturation process that extends from embryogenesis to the postnatal alveolarization period; it is characterized by cellular differentiation, extracellular matrix reorganization, alveolar septation, and an increase in surfactant synthesis. This structural and biochemical transformation, along with the thinning of the air-blood barrier and the rearrangement of parenchymal composition, leads to progressive changes in the mechanical properties of lung tissue. Consequently, fetal lung maturation is recognized not only as a morphological process

but also as a biomechanical one. Neonatal respiratory distress syndrome (RDS) remains a significant cause of morbidity and mortality, particularly in preterm births [1]. Traditionally, invasive tests based on amniotic fluid analysis (such as lecithin/sphingomyelin ratio and lamellar body count) have been utilized to evaluate fetal lung maturity [2, 3].

However, due to their invasive nature, these methods carry a risk of procedure-related complications, possess limited reproducibility, and their clinical applicability is steadily declining. In this context, there is an increasing need for imaging-based, non-invasive, safe, and reproducible biomarkers to assess fetal lung maturation. Shear wave elastography (SWE) is an ultrasound-based technique that quantitatively evaluates elasticity by measuring the propagation velocity of transverse waves generated in the tissue by an acoustic radiation force impulse [4, 5]. Values obtained via shear wave velocity or Young's modulus are accepted as numerical counterparts of the tissue's mechanical properties. This method, which has been clinically validated in various organ pathologies—primarily liver fibrosis—is increasingly being used in obstetrics to evaluate the biomechanics of the placenta and fetal organs [6, 7]. Recent clinical studies have reported that fetal lung elasticity values are measurable at different gestational weeks and may vary depending on the week of pregnancy [8, 9].

However, much of the existing literature relies on cross-sectional designs; comparing different fetuses at different gestational weeks cannot fully control for inter-individual

biological variation. Normative data identifying elasticity changes longitudinally in the same fetus, particularly during the late second and third trimesters of healthy pregnancies, remain insufficient. Furthermore, it has been reported that both central and peripheral placental stiffness increase in Trisomy 21 (T21) pregnancies, and central SWE measurements specifically are significant in predicting T21 independently of maternal age. Longitudinal evaluation of fetal lung elasticity may more reliably demonstrate the progression of biomechanical maturation according to gestational age and support the potential use of elastographic parameters as indicators of physiological development [10]. Nevertheless, during the application of SWE in fetal tissues, exposure duration, as well as thermal and mechanical indices, must be carefully controlled, and measurement protocols must be standardized.

Methods

This prospective, longitudinal observational study was conducted with the approval of the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (dated 27.12.2024, No: 24-MOBAEK-048). The study was carried out between January 2025 and June 2025 at the Tokat Gaziosmanpaşa University Hospital, and written informed consent was obtained from all participants. The primary endpoint of the study was the quantitative evaluation of the change in fetal lung elasticity values (Young's modulus, kPa; shear wave velocity, m/s) measured in the same fetus between 28–32 weeks and 35–38 weeks of gestation. The secondary endpoint was the description of fetal lung elasticity distributions in healthy pregnancies during the late second and third trimesters.

Study Population

Singleton and healthy pregnant women at or above 28 weeks of gestation who applied for routine obstetric follow-up were evaluated consecutively. Inclusion criteria included: singleton pregnancy of 28 weeks or more, absence of major fetal anomalies on detailed ultrasonography, absence of systemic or obstetric pathologies that could affect fetal lung development, and the ability to undergo measurements at two different gestational weeks in accordance with the study protocol. Exclusion criteria were determined as gestational diabetes, intrauterine growth restriction, oligo/polyhydramnios, congenital fetal anomalies, preterm birth, and failure to attend follow-up controls.

Based on these criteria, nine cases were excluded, and a total of 50 pregnant women who completed measurements at both time points were included in the final analysis. Gestational age was based on the last menstrual period (LMP) and confirmed in all cases by crown-rump length (CRL) measured in the first trimester. In cases where a difference of > 7 days was detected between LMP and CRL, the gestational week was rearranged according to CRL. This method was preferred to ensure accurate analysis of biomechanical changes related to gestational age. Participants were evaluated longitudinally at two time points: the first measurement between 28–32 gestational weeks and the second measurement between 35–38 gestational weeks. (Fig. 1A-B)

Schematic diagram of lung elasticity measurements. All measurements were performed in split-screen mode. A: Lung elasticity measurement at 30 weeks of gestation. B: Lung elasticity measurement at 36 weeks of gestation.

Ultrasonography and Elastography Protocol

All ultrasonographic and elastographic evaluations were performed by a single radiologist with five years of experience using a Philips Epiq Elite ultrasound system (Philips Healthcare, Bothell, USA) and a 1–5 MHz convex probe. Device parameters were standardized during measurements (mechanical index < 1.9; soft tissue thermal index ≤ 0.7; spatial peak temporal-average intensity < 720 mW/cm²), and the duration of elastography was limited to a maximum of 10 minutes per case.

Prior to measurement, standard fetal biometric and anatomical evaluations were performed; fetal position, placental location, and amniotic fluid volume were recorded. The most suitable imaging window for the fetal lung parenchyma was obtained via a lateral/proximal thoracic section, and a parenchymal segment showing homogeneous echogenicity was preferred. Two-dimensional shear wave elastography (2D-SWE) was applied using ElastoQ Imaging software. Measurements were selected from the areas of highest reliability, taking into account the reliability index on the color-based stiffness and velocity map generated by the software.

The ROI (Region of Interest) diameter was standardized at 5 mm and placed within the fetal lung parenchyma; large vascular structures, ribs, and pleural areas were excluded. The probe was contacted with the maternal skin using minimal and constant pressure, avoiding excessive compression. Measurements were repeated when significant fetal movement was detected. In each fetus, 3–5 independent measurements were taken from the same region; a wait time of 3–5 seconds between

measurements was allowed to ensure tissue relaxation. The average of these measurements was recorded as the final elasticity value. Values were reported as both Young's modulus (kPa) and shear wave velocity (m/s).

In cases where a technically suitable imaging window was obtained, measurements were taken from both lungs. During the analysis phase, the average of the right and left lung measurements was used to obtain a single value representing global parenchymal biomechanics. This approach was adopted to reduce variation caused by lateralization, in line with the symmetrical growth characteristics of the fetal lung and the preference for using average values in the literature. For measurements to be included in the analysis, the criterion of an interquartile range (IQR)/median ratio of < 30% was applied to increase the reliability of the elastography measurements. Having all measurements performed by a single operator aimed to minimize interobserver variation; interobserver reliability analysis was excluded from the scope of this study.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation (minimum–maximum). Percentile distributions (5th–95th) were calculated where appropriate. The normality of the data was evaluated using the Shapiro–Wilk test. Paired-sample t-tests were used for comparisons between 28–32 week and 35–38 week measurements. Effect size was calculated using Cohen's d coefficient. The relationship between gestational week and fetal lung stiffness was evaluated using Pearson correlation analysis. Linear regression analysis was performed to determine the magnitude of weekly change, and regression coefficients (β), standard errors, and p-values were reported. Post-hoc power analysis was performed based on the observed mean difference to evaluate the statistical power of the study. All statistical analyses were performed using SPSS 27 software, and $p < 0.05$ was considered statistically significant.

In the post-hoc power analysis based on the observed mean difference, the study's statistical power was found to be over 80% ($\alpha = 0.05$). This finding indicates that the change in elasticity observed in the longitudinal measurements was demonstrated with an adequate sample size.

Results

A total of 50 healthy pregnant women with a mean age of 28.3 ± 4.47 years (range: 20–40) were included in the study. The mean BMI of the participants was 28.94 ± 3.75 kg/m², and placental location was distributed as 60% anterior and 40% posterior. Of the fetuses, 52% were female and 48% were male. No cases of preterm birth or neonatal respiratory distress syndrome (RDS) were observed during the study. When all measurements were evaluated together, the mean fetal lung stiffness was 2.37 ± 0.50 kPa (1.3–3.77), and the shear wave velocity (SWV) was 0.87 ± 0.09 m/s (0.67–1.12). (Table 1)

Table 1
Demographic Characteristics and Fetal Lung Ultrasound Parameters of the Study Population

Variables	Overall (n = 50)	28–32 Weeks (n = 50)	35–38 Weeks (n = 50)	p-value
Maternal Characteristics				
Age (years)	28.30 ± 4.47 (20–40)	-	-	-
Height (cm)	163.34 ± 5.04 (155–175)	-	-	-
Weight (kg)	77.28 ± 11.32 (61–109)	-	-	-
BMI (kg/m²)	28.94 ± 3.75 (22.15–39.08)	-	-	-
Placental Location, n (%)				
Anterior	30 (60%)	-	-	-
Posterior	20 (40%)	-	-	-
Fetal Gender, n (%)				
Female	26 (52%)	-	-	-
Male	24 (48%)	-	-	-
Elastography Parameters				
Fetal Lung Stiffness (kPa)	2.37 ± 0.50 (1.30–3.77)	2.65 ± 0.41 (1.70–3.54)	2.09 ± 0.43 (1.30–3.77)	**< 0.001**
Shear Wave Velocity (m/s)	0.87 ± 0.09 (0.67–1.12)	0.91 ± 0.07 (0.74–1.07)	0.82 ± 0.08 (0.67–1.12)	**< 0.001**

Footnotes: BMI: body mass indeks, kPa: kilopascal, m/s: meters per second. Results are presented as follows: mean ± standard deviation [minimum;maximum]; $p < 0.05$ is significant.

Comparative Analysis by Gestational Week

In the longitudinal analysis, fetal lung stiffness averaged 2.65 ± 0.41 kPa in the 28–32 gestational week range, whereas this value was measured as 2.09 ± 0.43 kPa at 35–38 weeks. Similarly, shear wave velocity values were found to be 0.91 ± 0.07 m/s in the early measurement and 0.82 ± 0.08 m/s in the late measurement. A significant decrease was detected in both parameters as the gestational week progressed ($p < 0.001$ for both comparisons). The effect size of the observed decrease in stiffness was large (Cohen's $d > 1$), indicating that the difference is significant not only statistically but also clinically

and biomechanically. The average absolute decrease was approximately 0.56 kPa, pointing to a distinct mechanical reorganization in the fetal lung parenchyma between trimesters.

Correlation and Regression Analysis

A significant negative correlation was found between gestational week and fetal lung stiffness ($p < 0.001$). Similarly, a negative relationship was observed between gestational age and shear wave velocity. In the linear regression analysis, it was determined that each weekly increase in gestational age was associated with a decrease of approximately 0.07–0.09 kPa in fetal lung stiffness. This finding suggests that the decrease in elasticity values reflects a linear and progressive biomechanical maturation process.

Normative Distribution and Reference Intervals

In the 28–32 gestational week group, the mean stiffness was 2.65 ± 0.41 kPa, and the 95% confidence interval was calculated as 2.53–2.77 kPa. In this group, the 5th, 50th, and 95th percentile values were determined to be approximately 1.80 kPa, 2.60 kPa, and 3.40 kPa,

respectively. In the 35–38 gestational week group, the mean stiffness was 2.09 ± 0.43 kPa, and the 95% confidence interval was 1.97–2.21 kPa. In the same group, the 5th, 50th, and 95th percentile values were found to be approximately 1.40 kPa, 2.00 kPa, and 2.90 kPa, respectively. Comparing both gestational week intervals shows that the elasticity distribution shifts from higher percentiles toward lower values. This distribution pattern supports a change in fetal lung biomechanics in favor of maturation as pregnancy progresses from the late second trimester to the third trimester. (Fig. 2A-B)

A: Graph of velocity (m/s) values by week. B: Graph of stiffness (kPa) values by week.

Discussion

In this prospective longitudinal study, a significant and distinct decrease in fetal lung elasticity was demonstrated in the same fetus between 28–32 and 35–38 weeks of gestation in terms of both kPa and m/s parameters. This observed decline quantitatively reflects the biomechanical maturation process occurring in the fetal lung parenchyma as gestational age advances. The high effect size supports that the detected change is significant not only statistically but also biophysically.

Fetal lung development is a dynamic process starting in the embryological period and continuing until the postnatal alveolarization process [11]. Particularly during the canalicular and saccular stages, structural transformations such as increased surfactant synthesis, alveolar septation, interstitial matrix reorganization, and thinning of the air-blood barrier occur. During this process, changes in the collagen/elastin ratio, a decrease in fluid content, and parenchymal remodeling may lead to a decrease in the mechanical resistance of the tissue. The progressive decrease in elasticity values in our study is pathophysiologically consistent with this microstructural and biochemical reorganization and suggests that it may be a biomechanical counterpart of fetal lung maturation.

Shear wave elastography (SWE) is an ultrasound technique capable of quantitatively assessing the elastic properties of tissues and providing numerical data on Young's modulus or shear wave velocity [4, 5]. In recent years, it has been widely used to distinguish between benign and malignant lesions and to assess fibrotic changes in various organs such as the liver, pancreas, kidneys, thyroid, and lymph nodes [12, 13]. In obstetric applications, there has been an increase in studies focusing on the elastographic evaluation of placental, fetal liver, and fetal lung tissue [6, 14].

The feasibility and safety of fetal lung SWE were first demonstrated in experimental and pilot studies [15, 16, 17]. A study evaluated fetal lung and liver elasticity between 24 and 34 weeks of gestation and demonstrated the clinical feasibility of the method [18]. A study examined changes in fetal lung elasticity values according to gestational age between 24 and 39 weeks and demonstrated that elasticity trends change as gestational age progresses. Similarly, another study evaluated fetal lung development using two-dimensional SWE at different gestational weeks and reported that elasticity values exhibit changes dependent on gestational age [19]. However, most of these studies are based on cross-sectional designs and cannot fully account for inter-individual biological variation. One of the significant contributions of our study to the literature is that it demonstrates longitudinal changes by measuring the same fetus at two different gestational weeks. The majority of studies in the literature employ cross-sectional designs and compare different fetuses at different weeks [18].

In our study, demonstrating changes in elasticity in the same pregnant women provides a more direct reflection of biomechanical changes associated with gestational age by minimizing the influence of interindividual biological variation.

Traditional methods for assessing fetal lung maturation are invasive and are now used less frequently in clinical practice [2, 3]. In recent years, various imaging methods have been developed to assess fetal lung maturation noninvasively. These methods include MRI signal intensity ratio [20], gray-level histogram analysis [21], quantitative ultrasound tissue analysis [22, 23, 24], and pulmonary artery Doppler parameters [25]. However, most of these methods provide indirect parameters or have limitations regarding standardization. The advantage of SWE is that it provides quantitative and reproducible data directly related to tissue elasticity. This feature makes the method a potentially more objective tool for assessing biomechanical maturity. Studies in cases of late preterm birth have reported an association between elasticity values and neonatal respiratory morbidity [26]. They have shown that elasticity values are higher in cases where RDS develops. Additionally, there are studies reporting increased fetal lung and placental stiffness in pregnant women with gestational diabetes [10].

These findings suggest that increased elasticity values may be associated with immaturity or functional delay. Although no cases of neonatal RDS were observed in our study, the marked decrease in elasticity values in subsequent weeks supports the hypothesis that this may serve as a biomechanical indicator of fetal lung maturation.

In the normative distribution analysis, the determination of percentile ranges for gestational weeks 28–32 and 35–38 revealed preliminary reference elasticity distributions for the late second trimester and

third trimester. The shift of this distribution toward lower values in subsequent weeks supports a change in fetal lung biomechanics favoring maturation. However, these data should be interpreted not as diagnostic threshold values but as a descriptive framework of the distribution in healthy pregnancies.

Limitations

This study has several limitations. First, the relatively small sample size may limit the generalizability of the findings. Second, the fact that all measurements were performed by a single observer prevented the conduct of an interobserver reliability analysis. However, the application of the IQR/median < 30% quality criterion in the measurements was intended to enhance data reliability. Third, because no neonatal respiratory morbidity was observed in the study group, an elasticity-based diagnostic cutoff value could not be determined. Additionally, the fact that only healthy pregnancies were examined limits the ability to draw conclusions regarding high-risk groups.

Conclusion

In this prospective longitudinal study, a significant decrease in fetal lung elasticity was demonstrated in the same pregnant women between 28–32 and 35–38 weeks of gestation. This finding can be interpreted as a biomechanical reflection of gestational age-dependent structural and functional remodeling processes in the fetal lung parenchyma. 2D-SWE is a noninvasive and feasible method that allows for the quantitative assessment of fetal lung tissue when performed under appropriate safety parameters. However, the obtained values should be interpreted not as diagnostic thresholds, but as preliminary normative data describing longitudinal changes in healthy pregnancies. In the future, studies involving larger, multicenter cohorts and high-risk pregnancy groups will be critical for evaluating the correlation of elasticity parameters with neonatal respiratory morbidity, determining cutoff values, and conducting reproducibility analyses—all of which are essential for assessing the integration of SWE into clinical decision-making processes.

Declarations

Ethics approval and consent to participate

This prospective, longitudinal observational study was conducted with the approval of the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (dated 27.12.2024, No: 24-MOBAEK-048). The study was carried out between January 2025 and June 2025 at the Tokat Gaziosmanpaşa University Hospital, and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient confidentiality and institutional policies but are available from the corresponding author on reasonable request.

Competing interests

No potential conflict of interest was reported by the author(s).

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Author contributions

MEÖ responsible author, data collection, data analysis, content drafting. AHG study design, drafting. AAU data collection. MHA - MŞ draft revision. KK - HAK elastography measurement. FD final version approval.

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2025;53(5):654–61.

Figures

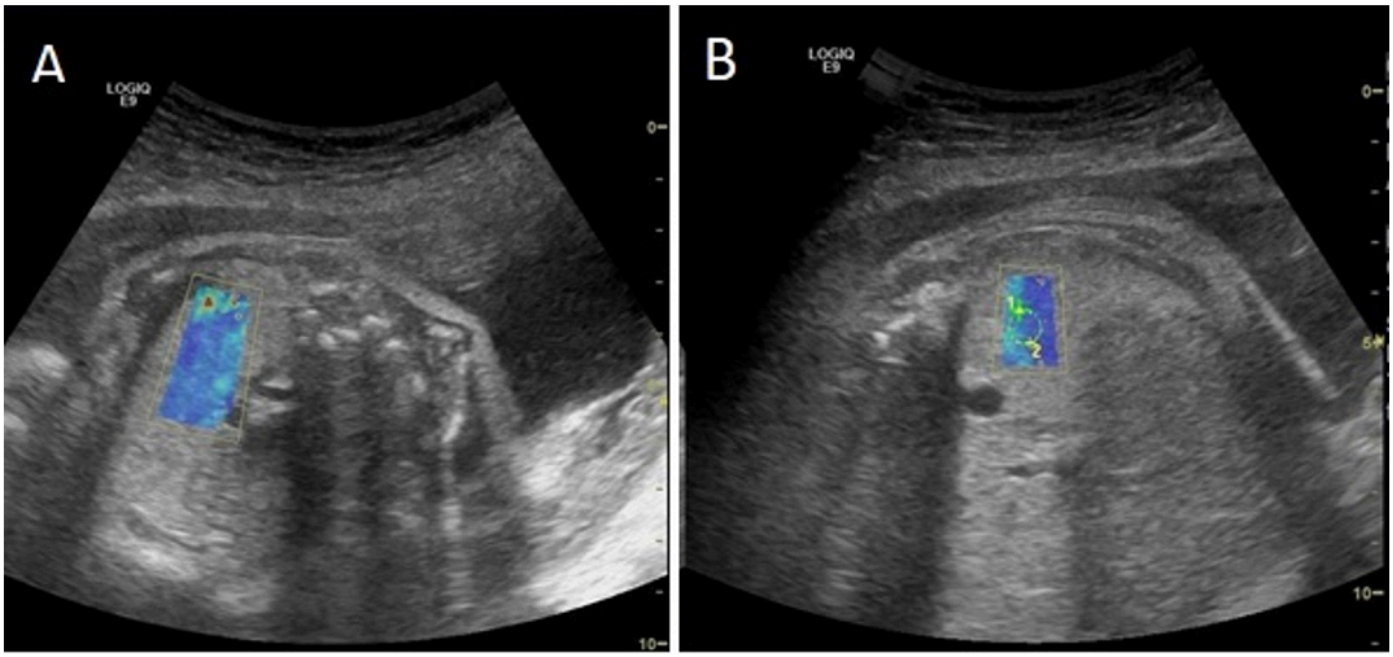


Figure 1

Real-time schematic display during fetal lung measurement.

Schematic diagram of lung elasticity measurements. All measurements were performed in split-screen mode. A: Lung elasticity measurement at 30 weeks of gestation. B: Lung elasticity measurement at 36 weeks of gestation.

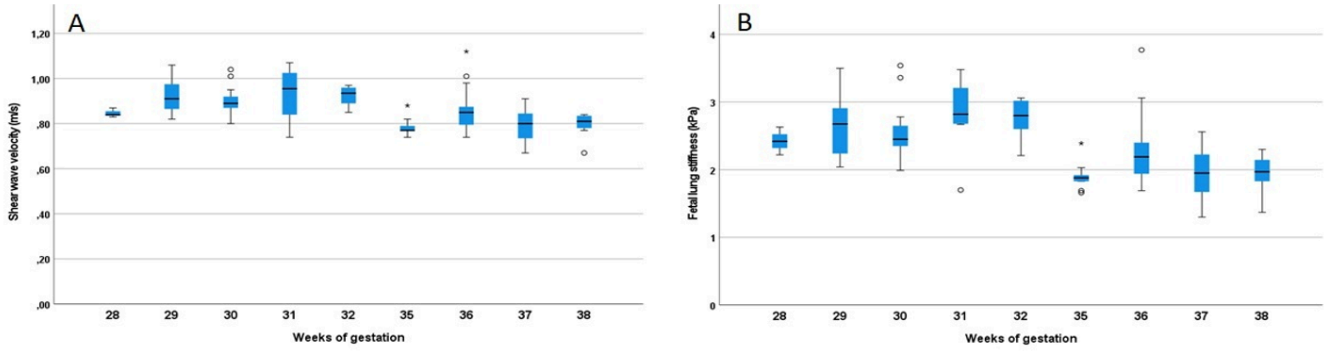


Figure 2

Graphs of fetal lung elasticity values by gestational week.

A: Graph of velocity (m/s) values by week. B: Graph of stiffness (kPa) values by week.