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Original Article

An Assessment of the Impact of Smoking and Vaping During Pregnancy on Placental Dysfunction Using Shear-Wave Elastography

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ABSTRACT

Objective: The primary variables influencing fetal growth are the genetic structure of the fetus, the functioning of the uteroplacental system, and maternal influences. The importance of smoking and exposure to cigarette smoke is a common preventable epidemiological problem. Smoking during pregnancy not only causes intrauterine growth restriction (IUGR) but also raises the chances of having other systemic gestational illnesses. This study aims to assess placental dysfunction and placental flexibility using sonoelastographic imaging in pregnant women who consume both conventional cigarettes and electronic cigarettes during the second trimester.

Methods: In 841 of the 1169 pregnancies included in the study, the placenta was located anteriorly, anterolaterally, or posterolaterally and analyzed by 2D-SWE elastography. In 328 pregnancies, the placenta was excluded from the study due to posterior uterine wall localization. In 2D-SWE elastography, a rectangular fixed region of interest (ROI) measuring 1 × 0.5 cm was positioned at both the center and edge of the placenta. The resulting quantitative value for placental stiffness was then shown on the B-mode sonogram.

Results: Our investigation revealed significant statistical disparities in the average placental elasticity values between pregnant women who smoked 10 or more cigarettes per day and those who did not smoke (χ^2: 22.61, $P < .001$). Our investigation did not find any statistically significant disparity in placental elasticity values between pregnant women who smoked traditional cigarettes and those who used electronic cigarettes ($P > .05$).

Conclusion: The adverse effects of smoking on fetal growth and development are thought to be caused by the presence of harmful substances in cigarette smoke and the formation of placental disorders. While 2D-shear wave elastography appears to be a dependable technique for examining uteroplacental dysfunctions and associated alterations caused by smoking and e-cigarette use during pregnancy, further extensive research studies are required.

Keywords: Smoking during pregnancy, uteroplacental dysfunction, placental elasticity, 2D-shear wave sonoelastography

INTRODUCTION

The primary determinants influencing the growth and development of the fetus are the genetic makeup of the fetus, the functioning of the uterus and placenta, and the environment in which the mother is situated. Smoking and exposure to cigarette smoke are significant factors that greatly influence fetal growth and development. These factors are noteworthy due to their high occurrence and the fact that they may be prevented.[1,2] Smoking during pregnancy not only leads to intrauterine growth retardation (IUGR) but also increases the risk of several pregnancy problems.

Smoking while pregnant has notable repercussions, such as impaired growth, increased risk of miscarriage, premature rupture of the amniotic sac, preterm birth, stillbirth, placenta previa, placental abruption, and sudden infant death syndrome (SIDS).[3] The importance of the placenta in the development of the embryo and fetus, as an organ that undertakes all of the metabolic functions carried out by many organs in

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postnatal life during the intrauterine period alone, cannot be discussed.[4,5]

Based on data provided by the World Health Organization (WHO), over 20% of women residing in industrialized nations engage in smoking, whereas roughly 9% of women in poor nations partake in this habit. The majority of these women persist in smoking during pregnancy. Carbon monoxide produced by smoking binds to hemoglobin and causes increased hypoxia in both mother and fetus. Prenatal exposure to carbon monoxide and hypoxia can lead to impaired placental blood flow and fetal growth restriction.[3,6]

The role of the placenta in fetal nutrition is very important. There is a close relationship between the size, structure, development, pathological lesions, and metabolic relations with the fetus and the transport and metabolic mechanisms of the placenta. In smokers, villi exposed to decreased uteroplacental blood flow show fixed characteristic disorders, and there is an increase in the number of villous trophoblastic cells with irregular thickening of the trophoblastic basement membrane. Mid-trimester uterine artery Doppler findings combined with the uterine artery resistance index and bilateral notches are currently the best methods for predicting the placental vascular risk of pregnancy. In the placental structures of pregnant smokers, an increase in villous cytotrophoblastic cells and irregular thickening of the progressive trophoblastic basement membrane are observed on light microscopy. In the placental structures of pregnant smokers, an increase in villous cytotrophoblastic cells and irregular thickening of the progressive trophoblastic basement membrane are observed on light microscopy.[7,8] Smokers have a decrease in blood flow to the uterus due to the constricting effects of nicotine and carbon monoxide on the blood vessels in the uterus. Placentas from smokers show a reduction in the proportion of capillaries and an increase in the thickness of the villous membrane compared to placentas from non-smokers or those who stopped smoking before getting pregnant. These alterations can lead to fetal growth retardation by reducing the gas exchange capacity of the placenta.

Subchorionic fibrin deposits and placental calcifications are more frequently observed in the placentas of smokers compared to non-smokers.[6-8] Yan Li and colleagues conducted an experimental investigation suggesting that exposure to cigarette smoking during pregnancy may result in elevated levels of free radicals and oxidative stress. These effects could potentially be linked to long-term neurotoxic consequences. Furthermore, recent studies have revealed that pregnant individuals are increasingly using electronic cigarettes (e-cigarettes) for several reasons. A higher percentage of female e-cigarette users are in the reproductive period between the ages of 20 and 28.[15]

The American College of Obstetricians and Gynecologists (ACOG) highlights the imperative importance of abstaining from smoking during pregnancy to safeguard the well-being of both the pregnant individual and the developing fetus. Pregnant women who continue to smoke often feel motivated to quit due to concerns about the negative effects on their pregnancy and childbirth outcomes. However, only half of pregnant women are able to quit smoking during the gestational period.[4]

Ultrasound elastography is a method employed to quantify alterations in the mechanical properties of parenchymal tissue that are linked to pathological processes. Over the past 10 years, researchers have also utilized this technique to examine alterations linked to uteroplacental dysfunction in the placenta. Doppler ultrasonography has been widely utilized to indirectly evaluate and characterize the extent of placental malfunction by assessing fetoplacental resistance indices. Two-dimensional shear wave elastography (2D-SWE) employs multiple acoustic force pulses to generate a 2-dimensional parametric color map of tissue stiffness, known as 2D-Shear Wave Elastography (2D-SWE). This technique enables the examination of specific regions within the color map to acquire precise measurements of tissue elasticity, which are then converted into kilopascals to represent elasticity values. 2D-SWE systems enhance the operator's ability to obtain more accurate elastography measurements by utilizing quality and propagation maps.[9,10]

MAIN POINTS

- Sonoelastography is a valuable imaging technique in radiology that is becoming increasingly useful for identifying diseases and aiding in diagnosis. It has been supported by significant studies.
- Several studies have demonstrated that both smoking and vaping can lead to microvascular harm and hinder the proper flow of blood through the placenta. Sonoelastography enables us to infer the stiffness of placental tissue and the vascular resistance that arises during vasculopathy.
- We believe that more studies are needed to establish a stronger role for sonoelastography in the fetoplacental circulation and in the measurement of placental tissue stiffness for diagnosis and follow-up.
- In the future, sonoelastography may serve as a supplementary diagnostic and follow-up imaging technique alongside Doppler ultrasound imaging. It can be used to assess vascular resistance and blood flow in systemic disorders that impact placental circulation, such as smoking.

Therefore, assessing the elasticity or rigidity of tissue enables the examination of the underlying pathophysiology in an organ. This imaging approach can accurately diagnose the extent and seriousness of hepatic fibrosis in individuals with liver cirrhosis. Sonoelastography is commonly employed in contemporary medicine to assess and classify chronic liver disease patients, as well as to evaluate breast and thyroid tumors.[14]

Placental sonoelastography is a recently developed area of research. In recent years, there has been a growing trend in the use of this technology in the field of obstetrics. Studies have specifically focused on examining the placentas of patients with preeclampsia.[11,12]

The American Institute of Ultrasound in Medicine (AIUM) has endorsed the safety of using 2D-SWE during pregnancy based on the research completed by Bamber and his colleagues in 2013. The AIUM has also certified that 2D-SWE has the same indications for usage as Doppler imaging.[13]

In this study, we investigated the presence of pathological findings that could affect fetal growth and development in the placentas of pregnant women who applied to our radiology clinic's obstetric ultrasound department for second-level detailed examination, by questioning smoking habits and exposure to cigarette smoke. We also examined the presence of placental dysfunction through the elasticity of the placenta using the 2D-SWE technique.

MATERIAL AND METHODS

The study was approved by the Erzincan Binali Yıldırım University Ethics Committee (Decision no: 2023.12/003-128.6, Date: 12/12 /2023) and conducted in accordance with the Helsinki Declaration. Due to the nature of the prospective study, we obtained the necessary agreement from the patients and shared the photographs in a fully anonymous way, guaranteeing that no patient's identity or personal information was revealed. Written informed consent was obtained from the patients who agreed to take part in the study.

The study took place from February 2023 to April 2024 at the Obstetric Ultrasonography Clinic, which is part of the Radiology department in a tertiary university hospital. It aimed to examine the smoking habits and exposure to secondhand smoke in pregnant women who applied for a detailed second-level obstetric ultrasonography between the 20th and 24th gestational weeks, based on their self-declarations. The research study included a cohort of 1169 pregnant women, aged between 17 and 48, with an average age of 24.8. Hundred and twenty-nine of these patients reported actively smoking during pregnancy or being exposed to secondhand smoke, whereas 33 reported using electronic cigarettes during pregnancy. The study group excluded pregnant individuals who were using medicine for a different purpose, had severe anemia and systemic connective tissue disease (such as SLE), high blood pressure, preeclampsia, heart illness, or a history of gestational diabetes. In addition, exclusion criteria were determined for those who had already undergone a cesarean section and for those with fetal anomalies such as anencephaly, hydrops fetalis, Chiari malformations, etc. The blood nicotine levels of the patients were not analyzed. Furthermore, a comprehensive second-level anomaly scan, along with Doppler ultrasonography and elastography, was conducted during the same session by a highly experienced radiologist with 19 years of expertise in these domains.

The pregnant women included in the study were categorized based on their smoking status.

I. Group: Non-smokers (cigarette -)
II. Group: Individuals who are exposed to cigarette smoke passively (passive smokers)
III. Group: Individuals who consume fewer than 10 cigarettes each day (cigarette < 10).
IV. Group: Individuals who smoke 10 or more cigarettes per day (cigarettes ≥10).
V. Group: Electronic cigarette users during pregnancy.

The CA1-7A convex transducer was utilized to perform B-mode ultrasonography and elastography on all patients while they were lying down in a supine position.

The Samsung/RS85 Prestige ultrasound system (Samsung Medison Co. Ltd. —Medical Systems Corporation, Gangwon-do 25108 Republic of Korea) was used to perform obstetric sonography, Doppler sonography, and elastography. The imaging was done with a 3.5-5 MHz convex transducer and the S-Detect™* (S-Shearwave Imaging) system, using the CA1-7A probe. Furthermore, all patients had color and power Doppler evaluation.

The study included a total of 1169 pregnancies, out of which 841 had placenta anterior, anterolateral, or posterolateral location. These pregnancies were investigated using 2D-SWE elastography. The 328 placentas were extracted due to their positioning on the posterior wall of the uterus. In 2D-SWE elastography, a rectangular fixed region of interest (ROI) of 1 × 0.5 cm was positioned both in the center and edge of the placenta. The B-mode sonogram then exhibited the quantitative value of placental stiffness. Special attention was given to placing the ROI in areas that were uniform, particularly in the axial

plane. The placental image was positioned centrally inside the field of view throughout the sonographic evaluation. The non-vascular core (sample 1) and peripheral (sample 2) regions of the placenta, located away from the cord insertion, were selected as the 2 sampling locations least influenced by fetal movements.

Five measurements were made from each region, from the central and peripheral edges of the placenta, and samples 1 and 2 were averaged and recorded. Patients were asked to hold their breath for 5 seconds during the measurements so that conditions affecting the signal-to-noise ratio would not interfere with the measurements.

During the process of sampling 1 and 2 and conducting measurements, precautions were taken to ensure that the ROI was not placed in vascular tissues or heterogeneous areas of the placenta. The researchers conducted 2D-SWE measurements at 2 locations in the placenta: the central region, which was 2 cm away from the umbilical cord insertion, and the peripheral region. They positioned the ROI, known as QBOX, in the area with the highest stiffness on the color map.

2D-SWE measurements were conducted in both the core region (2 cm away from the insertion of the umbilical cord) and the peripheral regions of the placenta. The ROI, known as QBOX, was positioned in the area with the highest stiffness on the color map. The measurement data, expressed in kilopascals (kPa), were automatically computed and presented for the full ROI. The mean elasticity values obtained from the measurements were utilized for statistical analysis, considering the SDs within each ROI.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20 for Windows, (IBM SPSS Corp.; Armonk, NY, USA). The data's normal distribution was assessed using the Kolmogorov-Smirnov test. Numerical variables that follow a normal distribution were represented using the mean and SD. Variables that did not follow a normal distribution were represented by their minimum and maximum values. Categorical variables were represented using numerical values and percentages. The statistical tests employed for comparing numerical variables between groups were the Student t-test and the Mann–Whitney *U*-test. The Fisher's exact test or Chi-square test was employed to compare categorical variables. Independent predictors were analyzed using multivariate logistic regression analysis. The independent diagnostic performance evaluation utilized ROC curve analysis. A 2-tailed *P*-value less than .05 was deemed to be statistically significant.

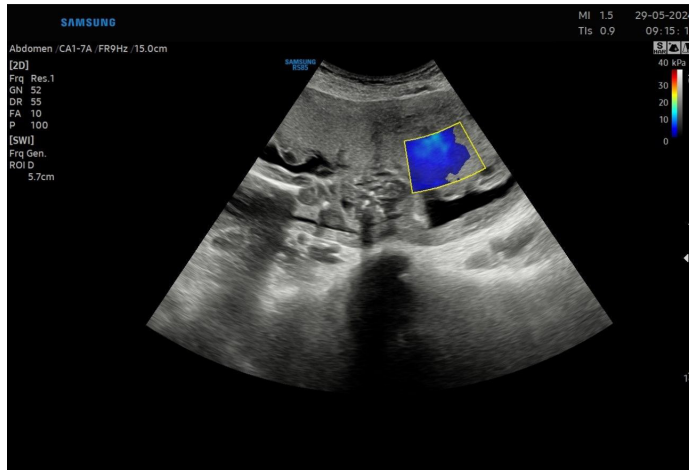

Figure 1. In a 25-year-old healthy primiviparity non-smoking pregnant woman with no known chronic disease, anteriorly located placental sonoelastographic evaluation showed low weight pascal values (kp value increases from blue to red on the bar colour scale).

RESULTS

The placenta's average elasticity values in all pregnancies in group I were 2.34 kPa at the center and 2.41 kPa at the edge, with a general average value of 2.48 kPa. There were no placental anomalies or disorders observed. Figure 1 depicts the patient in our study as an example case. The average elasticity values in group II, for pregnant women who were exposed to passive cigarette smoke, were 3.69 kPa at the center of the placenta and 4.76 kPa at the edge. The overall average value was 5.03 kPa. Figure 2 indicates the need for a sonoelastographic assessment of a patient who is exposed to secondhand smoking. In the group comparison test, the 2D-SWE intervals and mean

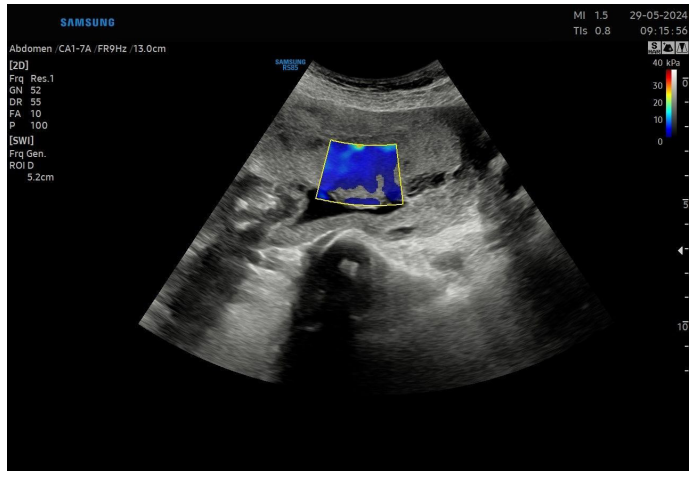

Figure 2. Placental sonoelastographic evaluation of a 34-year-old healthy, multiparous, active non-smoker but passive smoker with no known chronic disease showed anteriorly located low-weight pascal values (kp value increases from blue to red on the bar colour scale).

values in group I were substantially greater than those in group II ($P < .05$). Nevertheless, there was no statistically significant disparity observed in the measured elasticity values between the central and peripheral regions of the placenta ($P > .05$).

In group III, pregnant women who smoked less than 10 cigarettes a day had average elasticity values of 6.19 kPa and 7.43 kPa in the central and peripheral parts of the placenta, respectively. The overall average value was 6.82 kPa.

The mean elasticity values of the placentas in the central and peripheral areas of pregnant women who reported smoking 10 or more cigarettes per day in Group IV were 9.17 kPa and 11.28 kPa, respectively, with an overall mean value of 10.45 kPa.

In the group comparison test, the 2D-SWE intervals and mean values in this group were significantly higher than those in the other group ($P < .05$). Figure 3 presents patient images as an example for this group.

The mean elasticity values at the central region of the placenta for pregnant women in Group V who used electronic cigarettes were 8.79 kPa, whereas at the periphery it was 10.24 kPa, resulting in an overall mean value of 10.07 kPa. There was no statistically significant difference observed in the elasticity values assessed in the central or peripheral areas of the placentas of pregnant women in the IV and V groups ($P > .05$). Figure 4 depicts an illustration of a pregnant woman using an electronic cigarette.

In the statistical analyses performed on pregnant women who smoked cigarettes and electronic cigarettes, the difference in the increases in placental elasticity values was statistically significant. Intrauterine growth retardation was the most common complication related to smoking during pregnancy. The placental stiffness value in kilopascals was found to be statistically significantly higher in pregnant women who smoked 10 or more cigarettes per day compared to non-smokers (χ^2: 22.61, $P < .001$). No statistically significant difference was observed in placental elasticity values between pregnant women who smoked cigarettes and those who vaped ($P > .05$) in our study. Our findings of higher mean elasticity values in the central and peripheral parts of the placentas of pregnant women who were passively exposed to cigarette smoke and pregnant women who smoked cigarettes or electronic cigarettes were statistically significant (χ^2:13.18, $P < .001$; χ^2:10.70, $P < .05$; χ^2:10.90 $P < .05$, respectively).

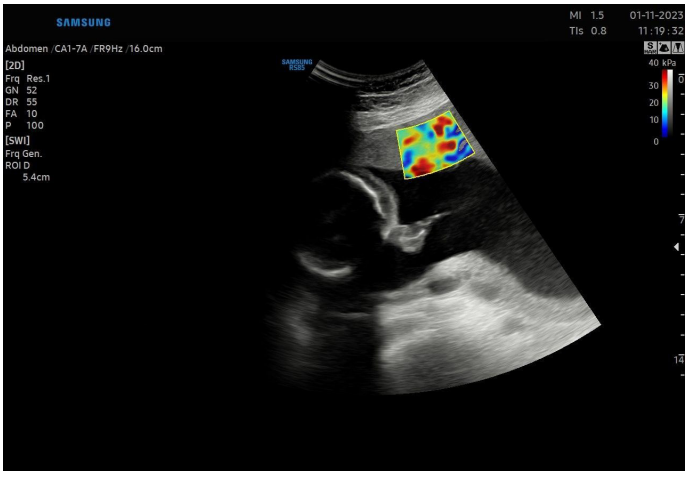

Figure 3. Placental elastography values in a 29-year-old pregnant woman with a 10 pack-year smoking history and no other chronic disease who was still an active smoker (kp value increases from blue to red on the bar colour scale).

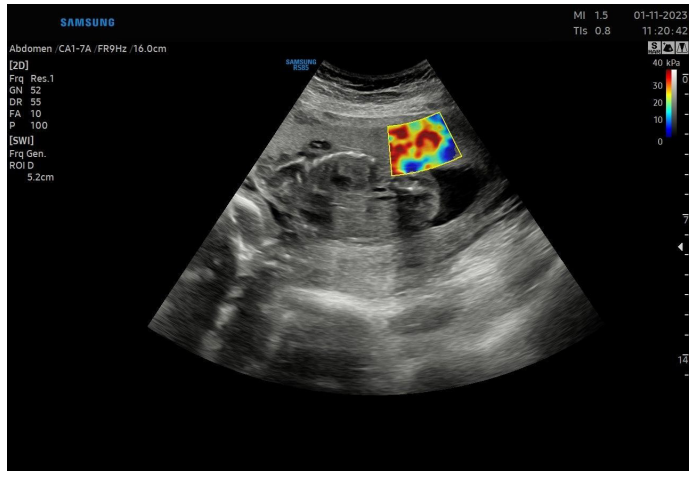

Figure 4. Placental elastography values in a 34-year-old pregnant woman with no known chronic disease, 10 pack-year smoking history and active vaping (kp value increases from blue to red on the bar colour scale).

DISCUSSION

The utilization of tissue elasticity imaging technology in clinical settings has spanned more than 2 decades, serving to evaluate the elasticity of parenchymal organs. 2D-SWE is an innovative method used to evaluate the elasticity of soft tissues. It offers a comprehensive understanding of the histological alterations occurring in tissues. As far as we know, there is no published study in the literature that specifically examines the elasticity of the placenta using 2D-shear wave elastography during the second trimester in pregnant women who smoke and vape. The findings of our study indicate that there are substantial differences in the 2D-SWE results and mean placental elasticity values throughout the second trimester between this group of pregnant women and normal pregnant women.[4,10]

Additionally, we found no disparity in mean placental elasticity values between peripheral and central regions. In 2012, Li et al found that there was no substantial disparity in the elastic modulus of the placenta between the periphery and central areas in a normal pregnancy. These findings indicate that both the placental center and periphery may serve as indicators of placental flexibility. These findings indicate that both the placental center and periphery may serve as indicators of placental flexibility.[15]

2D-shear wave elastography, a new method for tissue characterization, is useful for the assessment of placental function and can be used in addition to existing methods (Doppler and gray scale US) to investigate changes associated with uteroplacental dysfunction. Magnetic resonance elastography is known to play a role in the diagnostic algorithm of some parenchymal diseases, but its routine use in the assessment of placental elasticity is limited.[10,13]

One significant benefit of 2D-shear wave elastography is its ability to be conducted during the same session and using the same device as obstetric ultrasonography tests. Furthermore, a key benefit of this non-invasive process is its lack of reliance on the operator, as the 2D-SWE approach utilizes acoustic radiation force pulses and does not necessitate dynamic compression.[13,16]

In our experience, the need to hold the breath for about 5 seconds was not a problem for any patient. The only challenge for the radiologist performing the 2D-SWE was to set the ROI at the optimal placental site at a distance that would not be affected by fetal movements, which became unproblematic after a few cases.

Recent research conducted by Kılıç et al.[11] and Cimsit et al.[12] demonstrated that the rigidity of the placenta in preeclampsia patients was considerably greater than that of the control group.

Our investigation revealed a clear correlation between smoking during pregnancy and a higher occurrence of intrauterine growth restriction (IUGR) and pre-eclampsia. The risk of these complications was observed to rise in direct proportion to the quantity of cigarettes ingested. The negative impact of smoking on fetal growth can be attributed to the vasoconstrictor effects of nicotine and carbon monoxide, leading to fetal hypoxia. Additionally, smoking may cause placental pathologies that restrict the proper transport of nutrients to the fetus. Furthermore, smoking can adversely affect the release of certain hormones involved in fetal growth and development by affecting cyto- and syncytiotrophoblasts. Contrary to the claims of electronic cigarette manufacturers, it was also revealed that there was no statistically significant difference between the placental elasticity values in pregnant women who smoked cigarettes and electronic cigarettes included in this study.

Although 2D-shear wave elastography seems to be a reliable method to investigate all uteroplacental dysfunctions and related changes that may occur due to smoking and e-cigarette smoking during pregnancy, larger and more comprehensive research series are needed.

Ultrasonographic 2D-shear wave elastography is being used more frequently to evaluate the biomechanical characteristics of the placenta in cases where placental function is impaired. Smoking results in the breakdown of syncytiotrophoblasts, cytotrophoblasts, and fibrin-calcium deposits in the cotyledons. This, in turn, accelerates the development of the placenta, causing a reduction in its flexibility and a more rigid internal composition.[11,12]

This study had several constraints. Initially, pregnant women with placentas located on the posterior wall of the uterus were not included. Given that the maximum depth of penetration is 7-8 cm, this aspect can be understood as a technological constraint for the application of 2D-shear wave elastography in broad screening. Pregnant women may have been further categorized based on their age and the number of previous pregnancies. Nevertheless, a major constraint of our work is the inability to conduct histological analysis of placentas. Further research is required to investigate the relationship between placental histopathological alterations and the diagnostic effectiveness of this approach.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Erzincan Binali Yıldırım University (Date: 12.12.2023, Number: 2023.12/003-128.6).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Ö.D.; Design – Ö.D.; Supervision – T.Ç.; Resources – T.Ç.; Materials – T.Ç.; Data Collection and/or Processing – Ö.D.; Analysis and/or Interpretation – T.Ç.; Literature Search – Ö.D.; Writing Manuscript – T.Ç.; Critical Review – T.Ç., Ö.D.; Other – Ö.D.

Declaration of Interests: The authors have no conflict of interest to declare.

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