

The relationship of fetal adrenal gland size with fetal liver length and fetal abdominal wall fat thickness in mothers with and without gestational diabetes

Ensi khalili pouya

Shahid Beheshti University of Medical Sciences School of Medicine

Elham Keshavarz

Shahid Beheshti University

moein moradpour (✉ Moein.moradpour@gmail.com)

Shahid Beheshti University of Medical Sciences School of Medicine

Zahra ghomi

Shahid Beheshti University

Mehdi Eshaghzadeh

Shahid Beheshti University

mehdi khazaei

Shahid Beheshti University of Medical Sciences School of Medicine

shahnaz mohammadi

Shahid Beheshti University of Medical Sciences School of Medicine

farshid abolghasemzadeh

Shahid Beheshti University of Medical Sciences School of Medicine

hamideh zeidabadi

Shahid Beheshti University of Medical Sciences School of Medicine

Research Article

Keywords: gestational diabetes, fetus, adrenal gland, liver

Posted Date: February 23rd, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1332221/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Given the possible association between maternal diabetes status and metabolic disorders in the fetus, such as hepatic dysfunction or subcutaneous fat mass, it is expected that there is a close relationship between fetal adrenal gland volume and these two indicators.

Aim: We decided to examine the relationship of fetal adrenal gland size with fetal liver length and fetal abdominal wall fat thickness in mothers with gestational diabetes and also to compare it with non-diabetic mothers.

Methods: This cross-sectional study was performed on 40 pregnant women in the third trimester of pregnancy suffering gestational diabetes under insulin therapy as the cases and 40 age and gestational age-matched pregnant women without diabetes as the controls. An ultrasound was performed for all participants in the third trimester of pregnancy to assess adrenal gland size, liver dimensions and fetal abdominal wall fat thickness.

Results: The fetuses in diabetic group was found to have adrenal glands with significantly higher mean width, but with lower height leading similarity in mean adrenal volume as compared to non-diabetic group. The mean fetal abdominal wall fat thickness was significantly higher in diabetic than in non-diabetic groups. In diabetic groups, we found a direct association between height of adrenal gland and fetal abdominal wall fat thickness ($p = 0.001$). The length of adrenal gland was also positively associated with abdominal wall fat thickness ($p = 0.001$). However in non-diabetic group, we found no association between adrenal height and fetal abdominal wall fat thickness. Measuring liver length in the two groups showed significantly higher mean value in diabetic than in non-diabetic groups. No association was revealed between adrenal volume and liver length in diabetic group. In non-diabetic group, there was a significant direct association between adrenal volume and liver length ($p = 0.008$).

Conclusion: Gestational diabetes is directly associated with increasing fetal abdominal wall fat thickness and liver length in fetus. The dimensions of adrenal gland in fetus are also associated with fetus abdominal wall fat thickness and liver length probably independent to maternal diabetic status.

Introduction

Gestational diabetes with a prevalence of 1 to 14% in different parts of the world is one of the most common diseases that have attracted the attention of many researchers today. According to the World Health Organization (WHO) recent reports, the prevalence of this disease in the world is increasing. Some studies have estimated the prevalence of this disease between 3 and 6.1% in Iran (1, 2). This is while in other studies, its prevalence in Iran has been reported to be about 12% and it has been emphasized that the prevalence of gestational diabetes in our country is increasing (3). Various factors such as obesity, smoking, genetic background, family history, etc. are involved in the development of gestational diabetes. Recent studies have shown that gestational diabetes not only has a negative effect on maternal health but also leads to abnormalities in the fetus (4). Gestational diabetes is associated with a variety of

disorders and abnormalities in the mother and fetus, including cardiovascular problems, fetal macrosomia, birth defects, polyhydramnios, preeclampsia, neonatal metabolic disorders (hypoglycemia, hyperglycemia, and hypoglycemia) and respiratory distress (5–7). Due to the high prevalence and complications of gestational diabetes for both mother and fetus, screening for gestational diabetes is very important to prevent possible abnormalities in the fetus. Intermittent blood glucose measurements as well as regular ultrasounds play an important role in diagnosing, identifying and preventing the consequences of gestational diabetes on both mother and fetus.

Recent studies have shown that diabetes causes changes in fetal metabolic status that may be associated with fetal weight gain as well as tissue abnormalities (8). These metabolic changes can cause the liver and subcutaneous fat to grow disproportionately. Accordingly, some studies have examined the ultrasound of the abdominal circumference and subcutaneous fat around the arm as an index of estimating the weight and the impact of the fetus on the status of maternal diabetes (9). Additionally, some studies have examined the size of the fetal adrenal gland as another criterion in gestational diabetes (10). The fetal adrenal gland is a specific endocrine organ with an active role during fetal development that produces large amounts of steroids for estrogen biosynthesis. Steroid hormones produced by the adrenal glands regulate intrauterine homeostasis and fetal development and delivery time. Previous studies have shown that ultrasound evaluation of fetal adrenal size can be a reliable criterion for predicting preterm delivery (11). Some studies have also shown that significant changes in nutritional status such as malnutrition can alter the morphology and function of the adrenal glands in humans and animals (12). Given the role of the adrenal glands in fetal growth and development and the effects of maternal diabetes status on fetal metabolic status, it has recently been suggested that fetal adrenal volume may be related to maternal gestational diabetes status, although contradictory results are available in this regard. Moreover, given the possible association between maternal diabetes status and metabolic disorders in the fetus, such as hepatic dysfunction or subcutaneous fat mass, it is expected that there is a close relationship between fetal adrenal gland volume and these two indicators (liver parameters and subcutaneous fat thickness) in the fetus of diabetic mothers. Therefore, in the present study, we decided to examine the relationship of fetal adrenal gland size with fetal liver length and fetal abdominal wall fat thickness in mothers with gestational diabetes and also to compare it with non-diabetic mothers.

Materials And Methods

This cross-sectional study was performed on 40 pregnant women in the third trimester of pregnancy suffering gestational diabetes under insulin therapy as the cases and 40 age and gestational age-matched pregnant women without diabetes as the controls. Before the study, demographic information about participants including maternal age, gestational age, and history of any family illness was recorded. Those with having pre-pregnancy diabetes, existence of anomalies in the fetus, fetal IUGR or fetal infection, multiples in the present pregnancy, and dissatisfaction with continuing the study at any stage were all excluded from the study.

At first, the objectives of the study were presented to all patients and in case of agreement to participate in the present research project, written consent was obtained from them. Gestational diabetes screening was performed between 30 and 38 weeks of gestation using a 54-g 1-hour glucose loading test. One-hour glucose tolerance greater than 104 mg / dL was considered as the mother with gestational diabetes. The researcher prepared a questionnaire containing variables such as maternal age, gestational age, maternal weight, etc. After examining and selecting people with gestational diabetes treated with insulin and non-diabetics, an ultrasound was performed for all participants in the third trimester of pregnancy with a device (GE Voluson E6) with a curved transducer of 4 to 8 MHz. Only one ultrasound was performed for each patient by an experienced person. Also, for each participant, a routine pregnancy ultrasound including fetal anomaly screening and biometrics was performed initially. Adrenal gland dimensions and fetal liver length were measured specifically for the present study. The adrenal gland of the fetus was identified as a hypoechoic structure with an echogenic center located in the superior and medial position to the ipsilateral kidney. Adrenal gland close to the probe was selected for evaluation and angle and depth were adjusted to achieve the best image resolution. Then adrenal size was measured in three dimensions and the volume obtained by the device was considered as adrenal volume. Adrenal length was measured in the transverse plane, width in the coronal plane and depth in the sagittal plane. Each measurement was performed using the outer hypoechoic contour of the gland. To assess the size of the liver, its length was measured, so that the length of the right lobe of the liver was measured in the coronal plane from the diaphragm to the tip of the right lobe. Measurement of fetal abdominal wall fat thickness was performed in the standard AC measurement section of the largest abdominal wall fat thickness perpendicular to the abdominal muscles.

For statistical analysis, results were presented as mean \pm standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t test or Mann-Whitney test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. The association between the quantitative parameters was assessed using the Pearson's or Spearman's correlation tests. P values of ≤ 0.05 were considered statistically significant. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

Results

The results related to fetal abdominal wall fat thickness and adrenal volume

Table 1 compared baseline characteristics in diabetic (n = 40) and non-diabetic (n = 40) groups. We showed no difference across the two groups in terms of fetus gender (p = 0.588), fetus weight (p = 0.577), birth weight of neonates (p = 0.660), gestational age on sonography assessment (p = 0.740), mean mothers age (p = 0.086), but mean of mothers' weight was significantly higher in diabetic than in non-diabetic groups (p = 0.001). The fetuses in diabetic group was found to have adrenal glands with significantly higher mean width, but with lower height leading similarity in mean adrenal volume as compared to non-diabetic group ($2634.59 \pm 1146.33 \text{ mm}^3$ versus $2930.70 \pm 1598.73 \text{ mm}^3$, p = 0.344)

(Table 1). Also, the mean fetal abdominal wall fat thickness was significantly higher in diabetic than in non-diabetic groups ($7.41\pm 1.81\text{mm}$ versus $6.44\pm 1.32\text{mm}$, $p = 0.008$).

Table 1
The baseline characteristics in diabetic and non-diabetic groups (n = 80)

Parameters	Diabetic group	Non-diabetic group	P value
Baseline characteristics			
Fetus male gender, %	19 (47.5)	19 (47.5)	1.000
Mean fetus weight on sonography, gr	2304.62±671.08	2387.08±644.40	0.577
Mean birth weight, gr	3178.13±437.08	3219.13±392.61	0.660
Mothers' weight before pregnancy, kg	75.42±9.33	68.42±6.49	0.001
Mothers' weight within pregnancy, kg	83.92±8.73	76.85±6.13	0.001
Mean gestational age on sonography, wk	33.52±2.98	32.78±1.85	0.740
Mean mothers' age on sonography, year	32.85±5.89	30.55±5.94	0.086
Organ diameters			
Mean adrenal length, mm	14.45±3.60	15.50±3.34	0.230
Mean adrenal width, mm	21.52±4.09	18.90±4.13	0.006
Mean adrenal height, mm	16.55±4.02	18.40±4.19	0.048
Mean adrenal volume, mm ³	2634.59±1146.33	2930.70±1598.73	0.344
Mean fetal abdominal wall fat thickness, mm	7.41±1.81	6.44±1.32	0.008

In diabetic groups, we found a direct association between height of adrenal gland and fetal abdominal wall fat thickness ($p = 0.001$). The length of adrenal gland was also positively associated with abdominal wall fat thickness ($p = 0.001$). But the diameter of this gland was independent to other baseline parameters including fetal weight, birth weight of neonates, maternal weight before and during pregnancy, and mothers' age, and gestational age (Table 2). However in non-diabetic group, we found no association between adrenal height and fetal abdominal wall fat thickness ($p = 0.454$). In non-diabetic group, fetal abdominal wall fat thickness was correlated to fetal weight ($p = 0.039$), birth weight ($p = 0.009$), gestational age ($p = 0.028$), but not to other parameters. In diabetic ones, fetal abdominal wall fat thickness was correlated to fetal weight ($p = 0.001$), birth weight ($p = 0.008$), maternal weight before pregnancy ($p = 0.011$) and during pregnancy ($p = 0.007$), and gestational age ($p = 0.001$).

Table 2
The association of fetal abdominal wall fat thickness with other parameters in diabetic and non-diabetic groups (n = 80)

Parameters	Diabetic group	Non-diabetic group
Mean fetus weight on sonography, gr	0.001	0.039
Mean birth weight, gr	0.008	0.009
Mothers' weight before pregnancy, kg	0.011	0.265
Mothers' weight within pregnancy, kg	0.007	0.359
Mean gestational age on sonography, wk	0.001	0.028
Mean mothers' age on sonography, year	0.208	0.346
Mean adrenal length, mm	0.682	0.537
Mean adrenal width, mm	0.781	0.524
Mean adrenal height, mm	0.031	0.454

The results related to fetal liver length and adrenal volume

Of 80 women, liver dimensions were determined in 46 women (23 in diabetic and 23 in non-diabetic groups). Regarding baseline characteristics, 43.5% and 56.5 of neonates were male respectively with no difference ($p = 0.37$). The mean gestational age on sonography assessment time was also 33.52 ± 2.98 weeks and 32.78 ± 1.85 weeks respectively with no difference ($p = 0.31$). Also, no difference was found in mean of mothers' age (33.41 ± 6.63 years versus 30.00 ± 6.33 years, $p = 0.10$). The mean neonatal weight was also found to be 2.37 ± 0.65 kg and 2.13 ± 0.41 kg respectively indicating no difference ($p = 0.14$). In this regard, there was also no difference in birth weight between diabetic and non-diabetic groups (3.34 ± 0.40 kg versus 3.14 ± 0.33 kg, $p = 0.08$). Measuring liver length in the two groups showed significantly higher mean value in diabetic than in non-diabetic groups (0.55 ± 10.89 mm versus 49.04 ± 7.74 mm, $p = 0.03$). The average of fetal adrenal volume was similar in diabetic and non-diabetic groups (2.62 ± 1.28 cm versus 3.89 ± 1.32 cm, $p = 0.15$). As shown in Table 3, we found no difference between male and female fetuses in study parameters including embryo age, mother age, weight on sonography time, birth weight, liver length as well as adrenal volume. In diabetic groups, we showed no association of fetal adrenal volume or liver length with other fetal diameters (Table 4). Also, no association was revealed between adrenal volume and liver length in diabetic group. In non-diabetic group, there was a significant direct association between adrenal volume and liver length ($p = 0.008$). However, both parameters of adrenal volume and liver length were not associated with other fetal parameters (Table 2). In total and regardless of diabetes state, liver length was directly associated with embryo age ($p = 0.011$), but adrenal volume was associated with none of other fetal parameters (Table 2).

Table 3
The parameters in fetuses according to gender (n = 46)

Parameters	Male fetuses	Female fetuses	P value
Diabetic group			
Embryo age (weeks)	32.4 ± 3.74	34.38 ± 1.98	0.11
Mother age (Year)	34.25 ± 6.29	32.66 ± 7.21	0.63
Weight during sonography (Kg)	2.41 ± 0.82	2.34 ± 0.53	0.80
Weight at birth (Kg)	3.4 ± 0.34	3.29 ± 0.45	0.51
Liver length (mm)	54.2 ± 9.1	55.61 ± 12.43	0.76
Adrenal volume (cm3)	2.41 ± 1.36	2.79 ± 1.25	0.49
Diabetic group			
Embryo age (weeks)	33.0 ± 1.41	32.5 ± 2.36	0.53
Mother age (Year)	28.38 ± 7.17	32.10 ± 4.55	0.16
Weight during sonography (Kg)	2.15 ± 0.31	2.09 ± 0.52	0.74
Weight at birth (Kg)	3.23 ± 0.37	3.02 ± 0.24	0.13
Liver length (mm)	49.3 ± 4.1	48.7 ± 11.12	0.85
Adrenal volume (cm3)	3.12 ± 0.47	3.0 ± 0.93	0.67

Table 4
The association of adrenal volume and liver length with other fetal parameters (n = 46)

Parameters	Adrenal volume (p value)	Liver length (p value)
Diabetic group		
Embryo age (weeks)	0.48	0.06
Mother age (Year)	0.14	0.86
Weight during sonography (Kg)	0.80	0.07
Weight at birth (Kg)	0.92	0.17
Liver length (mm)	0.19	—
Adrenal volume (cm3)	—	0.19
Non-diabetic group		
Embryo age (weeks)	0.24	0.16
Mother age (Year)	0.34	0.18
Weight during sonography (Kg)	0.38	0.42
Weight at birth (Kg)	0.22	0.35
Liver length (mm)	0.008	—
Adrenal volume (cm3)	—	0.008
Total		
Embryo age (weeks)	0.68	0.011
Mother age (Year)	0.48	0.26
Weight during sonography (Kg)	0.68	0.12
Weight at birth (Kg)	0.64	0.23
Liver length (mm)	0.32	—
Adrenal volume (cm3)	—	0.32

Discussion

The results of our study showed that there is a significant difference in the mean fetal liver length between the two groups of diabetic and non-diabetic mothers. But no significant difference was observed in the mean adrenal volume of the fetus between diabetic and non-diabetic mothers. In the next stages of

the study, these results were examined between male and female fetuses in both diabetic and non-diabetic groups. Our results showed no difference in the results of these parameters including fetal age during ultrasound, maternal age, fetal weight during ultrasound, birth weight, liver length, and adrenal volume between girls and boys in both diabetic and non-diabetic groups. Also in this study, the relationship between adrenal volume and liver length with each other parameters in each of the diabetic and non-diabetic groups was evaluated separately. The results of our study showed that in the diabetic group there was no significant relationship between fetal adrenal volume and fetal age during ultrasound, maternal age, fetal weight during ultrasound, birth weight, and liver length. There was also no correlation between fetal liver length and fetal age during ultrasound, maternal age, fetal weight during ultrasound, neonatal birth weight, and adrenal volume in the diabetic group. While in the non-diabetic group, a significant relationship was observed between fetal adrenal volume and liver length. In summary, first, fetal liver length is affected by diabetic state in mothers and is larger than fetuses with non-diabetic mothers. Second, the association of liver length and adrenal volume was only found in non-diabetic group not in diabetic ones indicates that the relationship is not dependent on the mother's diabetic status. In this regard, several studies have evaluated these parameters in diabetic and non-diabetic mothers. In a study by Anderson et al (2008) (13), a significant relationship was observed between fetal liver length and fetal age as well as fetal abdominal circumference. Increased abdominal circumference and fetal age were significantly associated with increased liver length. In their study, increasing the age of the fetus was significantly associated with increasing the length of the fetal liver, which is in line with the findings of this study. In another study by Garcia-Flores et al (2017) (14), the average adrenal volume in 39 fetuses of diabetic mothers was examined. The results of their research showed that the adrenal volume in the fetus of diabetic mothers was significantly increased. On the other hand, adrenal volume was significantly associated with postpartum weight. In a previous study by Roberts et al (1994) (15), the average liver length in fetuses of diabetic mothers in the 18th and 36th weeks of pregnancy is significantly higher than usual that about 12% of diabetic mothers had fetuses with longer liver length than average. In another study by Mirghani et al. (2007) (16), the mean fetal liver length in diabetic mothers was 36 mm (32-37 mm), while in non-diabetic mothers it was 31 mm (30-33 mm), which was a significant difference between the two groups. Their results also showed that the increase in liver length was significantly associated with maternal fasting glucose levels as well as glucose 2 hours after meals. No significant relationship was observed between fetal liver length and other weight and gender parameters. Therefore, these researchers stated that the average fetal liver length in diabetic mothers is somewhat longer than non-diabetic mothers. The results of this research are in line with our research findings. In our study, fetal liver length in diabetic mothers was significantly longer than non-diabetic mothers. Therefore, the results of our research as well as other studies show that gestational diabetes is one of the risk factors associated with increased adrenal volume as well as increased liver length. However, in our study, unlike other studies, no significant difference in fetal adrenal volume was observed between diabetic and non-diabetic groups. But the probable reason for this is the lack of significant differences between fetal and neonatal weight of diabetic and non-diabetic mothers in our study. One of the positive points of our research is the comparison of these parameters between diabetic and non-diabetic groups, which was not done in most previous studies. Although the main mechanism by which

gestational diabetes leads to increased liver length or adrenal volume is not well understood, recent studies have shown that gestational diabetes increases the production and secretion of growth hormone due to increased insulin levels, resulting in the stimulus for fetal organomegaly (17). Fibroblast growth factors (FGFs) as well as insulin-like growth factors (IGFs) are among the growth factors that increase their production and secretion as a result of increased insulin and hyperglycemia, leading to increased fetal size as well as other disorders (18). Studies have shown that G EGF concentration in diabetic mothers is significantly increased, which is associated with significant changes in embryonic tissue EGF receptors and eventually nephrogenesis due to increased glucose concentration (19). Thus, as with macrosomia, fetal organs in mothers with gestational diabetes tend to grow abnormally that can lead to severe disorders in the baby. In addition, the relationship between fetal age and liver length that was reported in this study and other previous studies indicates that liver length can be a good diagnostic criterion in determining gestational age.

In the present study, there was a significant difference in the mean fat thickness of fetal abdominal wall between diabetic and non-diabetic groups. The fat thickness of the fetal abdominal wall was affected in diabetic mothers and was greater than the fat thickness of the fetal abdominal wall in non-diabetic mothers. Also, a significant relationship was observed between the height of the adrenal gland and the thickness of the fetal abdominal wall fat in the diabetic group. In a study by Turan et al (20), the relationship between gestational diabetes and adrenal volume was examined in 90 pregnant women. The results of their study showed that the adrenal volume of the fetus in 39 of the 90 cases of diabetic pregnant women was larger than normal. Therefore, these researchers suggested adrenal volume study as one of the risk factors for maternal diabetes. In another study by Larciprete et al (21), the thickness of fetal abdominal wall fat was assessed in two groups of diabetic and non-diabetic mothers. The results of this study showed that there is a significant difference in the mean thickness of fetal abdominal wall fat between diabetic and non-diabetic groups that the thickness of fetal abdominal wall fat in diabetic mothers is greater than the thickness of fetal abdominal wall fat in non-diabetic mothers. In total, it can be suggested fetal abdominal fat thickness is affected by diabetic status in diabetic mothers and is greater than fetal abdominal fat thickness in non-diabetic mothers. In this regard, fetal abdominal fat thickness is in parallel affected by fetal weight, and gestational age. It seems that the thickness of the abdominal wall fat is better than the adrenal volume of the fetus to evaluate the effect of diabetes on the fetus and also it seems that the effect of diabetes is on increasing the width and height of the adrenal gland and not the adrenal volume.

Conclusion

It can be finally concluded that gestational diabetes is directly associated with increasing fetal abdominal wall fat thickness and liver length in fetus. The dimensions of adrenal gland in fetus are also associated with fetus abdominal wall fat thickness and liver length probably independent to maternal diabetic status.

Declarations

Ethics approval and consent to participate:

The study was ethically approved by the Shahid Beheshti University of Medical Sciences

Consent for publication:

The authors gave their consent for the publication of identifiable details

Availability of data and materials:

The study data can be available for the editor if necessary

Competing interests:

Authors state no conflict of interest

Funding:

The study was fanatically supported by Shahid Beheshti University of Medical Sciences

Authors' contributions:

EKP and EK and MM designed the study planning, MM and ZG and ME collected the data, MK and SM analyzed the data, FA and HZ drafted the paper. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Acknowledgements:

The authors would thanks all the subjects participated in the project

References

1. Nazari Robati F, Khanjani N, Tabasi Nejad N, Rezabeigi davarani E, Mohseni M. The Prevalence of Gestational Diabetes and Factors affecting it in a Health Care Center. *Health-Based Res.* 2017;2(4):307–17.
2. Jafari-Shobeiri M, Ghojzadeh M, Azami-Aghdash S, Naghavi-Behzad M, Piri R, Pourali-Akbar Y, et al. Prevalence and Risk Factors of Gestational Diabetes in Iran: A Systematic Review and Meta-Analysis. *Iran J Public Health.* 2015;44(8):1036–44.
3. Badakhsh M, Daneshi F, Abavisani M, Rafiemanesh H, Bouya S, Sheyback M, et al. Prevalence of gestational diabetes mellitus in Eastern Mediterranean region: a systematic review and meta-analysis. *Endocrine.* 2019;65(3):505–14. doi:10.1007/s12020-019-02026-4.

4. Denney JM, Quinn KH. Gestational Diabetes: Underpinning Principles, Surveillance, and Management. *Obstet Gynecol Clin North Am.* 2018;45(2):299–314. doi:10.1016/j.ogc.2018.01.003.
5. Dervisoglu P, Kosecik M, Kumbasar S. Effects of gestational and pregestational diabetes mellitus on the foetal heart: a cross-sectional study. *J Obstet Gynaecol.* 2018;38(3):408–12. doi:10.1080/01443615.2017.1410536.
6. Li YX, Long DL, Liu J, Qiu D, Wang J, Cheng X, et al. Gestational diabetes mellitus in women increased the risk of neonatal infection via inflammation and autophagy in the placenta. *Med (Baltim).* 2020;99(40):e22152. doi:10.1097/MD.00000000000022152.
7. Ashwal E, Hod M. Gestational diabetes mellitus: Where are we now? *Clin Chim Acta.* 2015 Dec 7;451(Pt A):14-20. doi: 10.1016/j.cca.2015.01.021.
8. Herrera E, Desoye G. Maternal and fetal lipid metabolism under normal and gestational diabetic conditions. *Horm Mol Biol Clin Investig.* 2016;26(2):109–27. doi:10.1515/hmbci-2015-0025.
9. Tantanasis T, Daniilidis A, Giannoulis C, Tzafettas M, Dinas K, Loufopoulos A, et al. Sonographic assessment of fetal subcutaneous fat tissue thickness as an indicator of gestational diabetes. *Eur J Obstet Gynecol Reprod Biol.* 2010;152(2):157–62. doi:10.1016/j.ejogrb.2010.05.035.
10. Hetkamp T, Hammer K, Möllers M, Köster HA, Falkenberg MK, Kerschke L, et al. Fetal adrenal gland size in gestational diabetes mellitus. *J Perinat Med.* 2019;47(9):941–6. doi:10.1515/jpm-2019-0146.
11. Agarwal S, Agarwal A, Joon P, Saraswat S, Chandak S. Fetal adrenal gland biometry and cervical elastography as predictors of preterm birth: A comparative study. *Ultrasound.* 2018;26(1):54–62. doi:10.1177/1742271X17748515.
12. MacLaughlin SM, Walker SK, Kleemann DO, Sibbons JP, Tosh DN, Gentili S, et al. Impact of periconceptional undernutrition on adrenal growth and adrenal insulin-like growth factor and steroidogenic enzyme expression in the sheep fetus during early pregnancy. *Endocrinology.* 2007;148(4):1911–20. doi:10.1210/en.2006-0761.
13. Anderson NG, Notley E, Graham P, McEwing R. Reproducibility of sonographic assessment of fetal liver length in diabetic pregnancies. *Ultrasound Obstet Gynecol.* 2008;31(5):529–34. doi:10.1002/uog.5298.
14. Garcia-Flores J, Cruceyra M, Cañamares M, Garicano A, Espada M, Nieto O, et al. Sonographic Evaluation of Fetal Adrenal Gland in Gestational Diabetes. *J Ultrasound Med.* 2017;4:0278–4297.
15. Roberts AB, Mitchell J, Murphy C, Koya H, Cundy T. Fetal liver length in diabetic pregnancy. *Am J Obstet Gynecol.* 1994;170:1308–12.
16. Mirghani H, Zayed R, Thomas L, Agarwal M. Gestational diabetes mellitus: fetal liver length measurements between 21 and 24 weeks' gestation. *J Clin Ultrasound.* 2007;35:34–7.
17. McIntyre HD, Zeck W, Russell A. Placental growth hormone, fetal growth and the IGF axis in normal and diabetic pregnancy. *Curr Diabetes Rev.* 2009;5(3):185–9. doi:10.2174/157339909788920947.
18. Hill DJ. What is the role of growth hormone and related peptides in implantation and the development of the embryo and fetus. *Horm Res.* 1992;38(Suppl 1):28–34. doi:10.1159/000182567.

19. Amri K, Amri K, Freund N, Duong Van Huyen JP, Merlet-Bénichou C, Lelièvre-Pégorier M. Altered nephrogenesis due to maternal diabetes is associated with increased expression of IGF-II/mannose-6-phosphate receptor in the fetal kidney. *Diabetes*. 2001;50:1069-.
20. Turan OM, Turan S, Funai EF, Buhimschi IA, Campbell CH, Bahtiyar OM, et al. Ultrasound measurement of fetal adrenal gland enlargement:an accurate predictor of preterm birth. *Am J Obstet Gynecol*. 2011;204(4):311.e1-10.
21. Larciprete G, Valensise H, Vasapollo B, Novelli GP, Parretti E, Altomare F, et al. Fetal subcutaneous tissue thickness (SCTT) in healthy and gestational diabetic pregnancies. *Ultrasound Obstet Gynecol*. 2003;22(6):591–7.