BMC Pregnancy and Childbirth

RESEARCH

Open Access

Gestational diabetes and its effect on fetal thymus size: a case–control study

Nasrin Mansouri[1], Erfan Khezripour[2], Niko Rashtiani[3], Marzieh Bagherinia[4] and Ali Azizi[5*]

Abstract

Introduction Fetal thymus size has recently been recognized as a sensitive parameter linked to pregnancy complications. This study investigates whether maternal diabetes affects fetal thymus size, potentially offering a means to identify at-risk fetuses before birth.

Methods This study was designed as a case–control study conducted from September 2023 to November 2024 in Iran. The study samples included 112 diabetic women (gestational diabetes or pre-pregnancy diabetes) as the case group and 112 healthy pregnant women attending the same hospital as the control group. Data were collected using a researcher-designed demographic questionnaire, and fetal thymus size was measured via abdominal ultrasound. Fetal thymus size is calculated using the thymic-thoracic ratio (TTR) and the thymus circumference.

Results A statistically significant difference was observed between the two groups regarding body mass index (BMI), an obstetric and demographic variable. The thymic-thoracic ratio (TTR) and the thymus circumference in diabetic pregnancies were statistically significantly lower than in the control group ($p=0.000$). Odds ratios (95% CI) for the TTR index were 0.61 (CI 95%: 0.48 to 0.78), and thymus circumference was 0.95 (CI 95%: 0.93 to 0.97).

Conclusion The present study indicated that a reduction in fetal thymus size may be associated with diabetes in pregnant women. However, it remains to be determined whether ultrasound evaluation of fetal thymus size can help predict perinatal outcomes in diabetic women.

Keywords Diabetes, Gestational, Pregnancy, Prenatal diagnosis, Thymus gland, Ultrasonography, Prenatal

Introduction

With the global rise in obesity, the prevalence of gestational diabetes (GDM) has also increased, affecting approximately 14% of all pregnancies worldwide [1], and reaching nearly 26% in populations of women at high risk for GDM [2]. The worldwide prevalence of this disorder varies based on the population studied and the diagnostic criteria applied [3]. The degree of hyperglycemia largely determines the maternal and fetal risks associated with diabetes during pregnancy. These risks include spontaneous miscarriage, pregnancy-induced hypertension [4], increased cesarean section rates [5], delivery-related injuries due to fetal macrosomia, fetal anomalies, asphyxia, and neonatal hypoglycemia [6]. Moreover, gestational diabetes increases the risk of obesity, hypertension, and

*Correspondence:
Ali Azizi
aliazizi@kums.ac.ir
[1] Department of Obstetrics and Gynecology, Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[2] Department of Radiology, Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[3] Department of Obstetrics and Gynecology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
[4] Clinical Research Development Center, Motazedi Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[5] Department of Community and Family Medicine, School of Medicine, Kermanshah University of Medical Sciences, Boulevard - St. University - School of Medicine, Kermanshah 6714869914, Iran

type 2 diabetes later in life for the offspring of these women [7].

During pregnancy, fasting serum insulin levels physiologically double due to the development of insulin resistance [8]. Insulin resistance begins in the mid-pregnancy phase and progresses through the third trimester. Less insulin sensitivity may be caused by more hormones that cause diabetes, like placental lactogen, progesterone, and cortisol, although the precise mechanisms underlying these changes remain incompletely understood [9]. On the other hand, increased lipolysis in pregnant women reduced physical activity, and increased caloric intake accelerated the development of insulin resistance [10]. Risk factors for gestational diabetes include maternal age, abnormal body mass index (BMI), a family history of overt diabetes, and belonging to ethnic groups with a high prevalence of diabetes [11, 12].

The anatomical and physiological adaptations of the mother are essential for the implantation of a healthy fetus and fetal development, with the maternal immune response playing a crucial role in achieving these adaptations [13]. The thymus and the T lymphocytes and regulatory T cells it produces play a significant role in this immune response. The thymus is a key organ that optimizes immune system function throughout life [14, 15]. Ultrasound can non-invasively observe the fetal thymus, which is typically located in the anterior mediastinum near the large arteries and the superior vena cava [16]. Given the dynamic nature of the thymus during fetal development, several factors can alter its cellular pattern before birth. Several studies have shown that the thymus shrinks during the prenatal period in cases of fetal abnormalities, intrauterine growth restriction, preterm birth, preeclampsia, and chorioamnionitis [17]. In this context, the relationship between maternal diabetes and fetal thymus size has also been explored. Hypoxic and metabolic stress resulting from impaired glucose metabolism during pregnancy may affect the size of the fetal thymus [18]. Limited studies have examined these characteristics, yielding conflicting results that underscore the need for further investigation. Karasin et al. [19] and Sinaci et al. [20] found smaller thymus sizes in fetuses of diabetic mothers. In contrast, Gok et al. [21] found no differences in thymus size between diabetic women and the control group. Various studies have also used different indices to measure fetal thymus size.

Based on previous research, a malfunctioning thymus might cause changes in the production of different inflammatory immune cells and cytokines that control insulin resistance. This, in turn, could make diabetes and its complications more likely to happen. Therefore, the thymus may be a key factor in diabetes and its related complications, and improving its function could be a promising therapeutic strategy for diabetic patients from birth onward. Given the recent recognition of fetal thymus size as a sensitive parameter associated with pregnancy complications, we conducted this study to explore the potential impact of maternal diabetes on fetal thymus size. Our findings suggest that assessing thymus size in pregnant women may help identify fetuses at risk for adverse outcomes such as preterm birth, intrauterine growth restriction, and neonatal morbidity. Furthermore, the influence of maternal diabetes on fetal thymus size underscores its potential impact on fetal immune system development, which may have long-term implications for neonatal health.

Methods

Study settings and participants

We conducted this case–control study at Imam Reza Hospital in Kermanshah from September 2023 to November 2024. Imam Reza Hospital, an educational and tertiary care center affiliated with Kermanshah University of Medical Sciences, provides specialized care for high-risk pregnancies and is equipped with advanced diagnostic and therapeutic facilities. We selected the participants using a convenience and purposive sampling method from pregnant women attending this medical center. The Student Research Committee of Kermanshah University of Medical Sciences approved all phases of this study under the ethics code IR.KUMS.MED.REC.1402.090. The study samples included 112 diabetic women (gestational diabetes or pre-pregnancy diabetes) as the case group and 112 healthy pregnant women attending the same hospital as the control group.

Pregnant women met the following inclusion criteria: gestational age between 19 and 37 weeks, single pregnancy, absence of fetal anomalies confirmed (Through a comprehensive two-stage screening process. In the first trimester, screening included ultrasound and blood tests, such as nuchal translucency (NT) measurement and maternal serum markers (e.g., PAPP-A and free β-hCG). In the second trimester, a detailed anomaly scan was performed, including assessments of fetal anatomy, biometry, and Doppler studies, as per standard obstetric protocols), lack of intrauterine growth restriction, macrosomia, polyhydramnios or oligohydramnios, premature rupture of membranes, preterm labor, no use of corticosteroids during pregnancy, no smoking, tobacco, or alcohol use, no chronic diseases such as hypertension, liver disease, kidney disease, or coagulation disorders, and a willingness to participate in the study. Medical history and laboratory tests led to the diagnosis of diabetes in the case group.

Gestational diabetes traditionally defined as glucose intolerance first detected or diagnosed during pregnancy.

A more contemporary definition, and that used by the American Diabetes Association (ADA), is diabetes diagnosed after 15 weeks of gestation that was not clearly overt diabetes prior to conception [22]. This definition excludes patients diagnosed in early pregnancy because they likely have previously undiagnosed type 2 diabetes. Accordingly, if the patient's test results in weeks 24–28 of pregnancy showed a glucose challenge test (GCT) result of more than 140 or fasting blood sugar (FBS) level greater than 126 after the first trimester, serves as an indication for further testing with OGTT (100 g or 75 g). If the OGTT test is abnormal, the patient is diagnosed with gestational diabetes. Overt diabetes or pre-pregnancy diabetes: The individual has it before pregnancy, and it is diagnosed before or at the beginning of pregnancy (first trimester of pregnancy). The control group consisted of healthy pregnant women who met the inclusion criteria and had normal blood glucose levels. Before starting the study, we obtained informed written consent from all selected individuals, assuring them of the confidentiality of their data and their ability to withdraw from it at any stage.

The sample size was calculated using the G-power software based on the study by Dornemann et al. [23], with an odds ratio (OR) of 0.69 (31% reduced odds of smaller fetal thymus size based on the thymic-thoracic ratio (The thymic-thoracic ratio (TTR) was estimated as the ratio of the transverse diameter of the thymus to the thoracic diameter at the level of the three-vessel tracheal view) index in the diabetic group compared to the control group), $\alpha = 0.05$, power = 80%, and a 1:1 ratio for the study groups. The total sample size was calculated as 224, and with equal numbers in both groups, the final sample size for each group was set at 112 participants.

Data collection

Data was collected using a researcher-designed demographic questionnaire, and fetal thymus size was measured via abdominal ultrasound. Due to the asymmetrical shape of the thymus gland, there are various methods to measure it. This study used the thymic-thoracic ratio (TTR) and the thymus circumference measured in millimeters. TTR is a reproducible and practical method not influenced by body mass index (BMI), fetal gender, twin pregnancy, or gestational age [24]. The thymic-thoracic ratio was estimated by dividing the anteroposterior thymic and the intrathoracic mediastinal diameter. The distance from the transverse aortic arch border to the posterior chest wall was measured to evaluate the anteroposterior diameter. The intrathoracic mediastinal diameter is described as the length of a parallel line extending from the anterior edge of the thoracic vertebral body, passing through the center of the aortic arch vessel, to the interior margin of the sternum. All ultrasound measurements were performed at the level of the three-vessel tracheal view, which provides a standardized and reproducible approach for assessing fetal thymus size. To prevent measurement errors, all measurements were taken by a single experienced sonographer in the presence of an obstetrician.

Statistical analyses

Data analysis was performed using SPSS version 24 and Stata version 14. The independent t-test was used for quantitative variables, and chi-square, Fisher's exact test, and Linear- by- linear chi-square for trend were used for qualitative variables to compare demographic variables between the two groups (diabetes and control group). A comparison of thymus size between the study groups was conducted using one-way ANOVA. Logistic regression models were used to determine the association between diabetes and fetal thymus size while controlling for confounding factors. Finally, receiver operating characteristics (ROC) analysis was applied to examine the diagnostic value of the TT-ratio and thymus circumference for differentiation between diabetes pregnancy and normal pregnancy. Youden's index was used to determine a possible cut-off point. A significance level of 0.05 was considered for all analyses.

Results

Comparison of demographic and obstetric characteristics between diabetic and control groups in Table 1. The mean age of women in the diabetic group was 30.9 ± 3.4 years, and in the control group, it was 30.4 ± 3.4 years. The mean gestational age in the diabetic group was 30.6 ± 2.9 weeks; in the control group, it was 30.2 ± 3.9 weeks. There was a statistically significant difference between the two groups only in terms of body mass index (BMI) as an obstetric and demographic variable.

The comparison between the study groups, which included different types of diabetes (overt diabetes, insulin-dependent gestational diabetes, non-insulin-dependent gestational diabetes), and the control group in terms of fetal thymus size (using both TTR and thymus circumference indices) was conducted using one-way ANOVA. In this study, women's body mass index (BMI) was calculated based on their weight and height at the time of admission and was not based on pre-pregnancy or first-trimester levels. On the other hand, various studies have shown that BMI does not affect fetal thymus size, so when comparing the mean thymus size in the study groups, the effect of this variable as a confounder was not controlled. The result of this analysis showed that there was a statistically significant difference between all types of diabetes groups and the control group. This difference

Table 1 Comparison of socio-demographic and obstetrics characteristics of maternal diabetes cases and control group

Variables	Diabetes group ($n=112$)	Control group ($n=112$)	*p*-value
Maternal age (year)	30.9 ± 3.4	30.4 ± 3.4	0.263[a] t = −1.12
Gravidity	2.0 ± 1.2	1.9 ± 0.9	0.218[a] t = −1.23
1	48 (42.9%)	47 (42.0%)	0.088[b] $Chi^2=0.15$
2	26 (23.2%)	39 (34.8%)	
< = 3	38 (33.9%)	26 (23.2%)	
Abortion history			
No	81 (72.3%)	88 (78.6%)	0.352[b] $Chi^2=0.87$
Yes	31 (27.7%)	24 (21.4%)	
Stillbirth history			
No	100 (89.3%)	105 (93.8%)	0.337[c] $Chi^2=0.92$
Yes	12 (10.7%)	7 (6.3%)	
Number of children	0.6 ± 0.8	0.5 ± 0.7	0.341[a] t = −0.95
The last type of delivery			
Nil	58 (51.8%)	61 (54.5%)	0.619[b] $Chi^2=0.96$
Vaginal	26 (23.2%)	29 (25.9%)	
Cesarean section	28 (25.0%)	22 (19.6%)	
Body mass index (BMI, kg/m^2)	31.8 ± 3.6	29.8 ± 2.7	**0.000[a]** t = −4.73
Gestational age at the time of study (weeks)	30.6 ± 2.9	30.2 ± 3.9	0.403[a] t = −0.84
Education			
Illiterate /Elementary school	31 (27.7%)	23 (20.5%)	0.551[d] $Chi^2=2.87$
Guidance/ High school	36 (32.1%)	46 (41.1%)	
Diploma	38 (33.9%)	34 (30.4%)	
Academic	7 (6.3%)	9 (8.0%)	
Fetal thymus			
Circumference (mm)	71.9 ± 15.5	89.1 ± 19.5	**0.000[a]** t = 7.30
Thymic-thoracic ratio (TTR)	0.311 ± 0.09	0.472 ± 0.14	**0.000[a]** t = 10.11

Univariate *p*-values are from Independents sample test

[a] Chi-square test

[b] Fisher's exact tests

[c] Linear- by - linear Chi-square test

[d] *p*-value < 0.05 was considered statistically significant

in mean values was most pronounced in the overt diabetes group (MD = −0.179, CI 95%: −0.238 to −0.120, $p=0.000$) (Table 2).

Logistic regression analysis to determine the relationship between diabetes and fetal thymus size, both univariate and multivariate were performed. According to the regression analysis, for every 0.1 decrease in the TTR index, with an odds ratio (95% CI) of 0.61, the odds of diagnosing diabetes increased by 39%.

Based on the fetal thymus circumference index, for every 1-mm decrease in thymus circumference size, with an odds ratio (95% CI) of 0.95, the odds of diagnosing diabetes increased by 5% (Table 3).

The ROC curve was used to examine the diagnostic accuracy of thymus size in diagnosing diabetes based on both indices. The area under the ROC curve (AUC) for reviewing the predictive accuracy of thymus size based on the TTR index was 0.776, which, according to this analysis, is the best cutoff point for diagnosing diabetes in pregnant women with the highest sensitivity of 80.35% and specificity of 74.55% was 0.395. This study for the thymus circumference resulted in an area under the curve (AUC) of 0.243 with a sensitivity of 43.75% and a specificity of 21.43%, resulting in a numerical value of 23.70 as the cutoff point (Table 4, Figs. 1 and 2).

Discussion

This case–control study aimed to evaluate the relationship between gestational diabetes and changes in fetal thymus size. Our study showed that in diabetic women, compared to healthy women, the thymus size decreased in both indices, the thymic-thoracic ratio (TTR) and thymus circumference, and a statistically significant association was found between diabetes and reduced thymus size. However, in the thymus-to-chest ratio index, with an OR of 0.61, this association was stronger than the thymus circumference index, as the OR in the interpretive region was in the moderate effect range. In contrast, the result based on the thymus circumference index indicated a low effect size. Additionally, the decrease in thymus size in different types of diabetes (overt diabetes, insulin-dependent gestational diabetes, and non-insulin-dependent gestational diabetes) was more pronounced in the overt diabetes group compared to the control group. While previous studies have examined fetal thymus size in diabetic pregnancies, our study differentiates itself by providing a more detailed comparison of these two indices and highlighting the greater diagnostic accuracy of the TTR.

Overall, several methods exist for ultrasonography measurement of fetal thymus size. However, which method is the best for diagnosing maternal and fetal diseases is unclear. In one study, the transverse diameter of the fetal thymus, thymic-thoracic ratio, and thymus circumference were assessed in uncomplicated pregnancies. Based on the study results, they reported that the transverse diameter of the thymus was more suitable for clinical use in uncomplicated pregnancies [25]. However, several studies have reported that the thymic-thoracic ratio is more appropriate, as it is not affected by BMI or fetal gender and remains consistent throughout pregnancy [23, 26–28]. We used the TTR and thymus

Table 2 Comparison of fetal thymic-thoracic ratio (TTR) and circumference between different diabetes groups and control group

Thymus size	Overt Diabetes (*n* = 45)	Insulin-dependent gestational diabetes (*n* = 34)	Non-insulin dependent gestational diabetes (*n* = 33)	Control group (*n* = 112)	*p*-value
Thymic-thoracic ratio (TTR)	0.292 ± 0.08	0.316 ± 0.09	0.333 ± 0.08	0.472 ± 0.14	0.000
Circumference (mm)	64.7 ± 12.9	74.2 ± 16.8	79.0 ± 13.5	89.1 ± 19.5	0.000

P-values are from one-way ANOVA

Data presented as mean ± standard deviation

p-value < 0.05 was considered statistically significant

Table 3 Results of the logistic regression for maternal diabetes. Including thymic-thoracic ratio (TTR), circumference, and BMI as influencing factors

	Crude OR[a] (CI95%)	*p*-value	Adjusted OR[b] (CI95%)	*p*-value
Thymus-thoracic ratio (x + 1 vs. x units)	0.61 (0.48 to 0.78)	0.000	0.59 (0.45 to 0.77)	0.000
Circumference (mm)	0.95 (0.93 to 0.97)	0.000	0.94 (0.93 to 0.96)	0.000

p-value < 0.05 was considered statistically significant

[a] Odds ratio

[b] Adjusted for body mass index (BMI)

Table 4 Optimal cut-off values of the TT-ratio and circumference to predict diabetes determined by Youden's index

	Cut-off value	Sensitivity	Specificity	AUC	Youden's index
Thymus-thoracic ratio (TTR)	0.395	80.35%	74.55%	0.776	0.549
Circumference (mm)	70.23	43.75%	21.43%	0.243	0.349

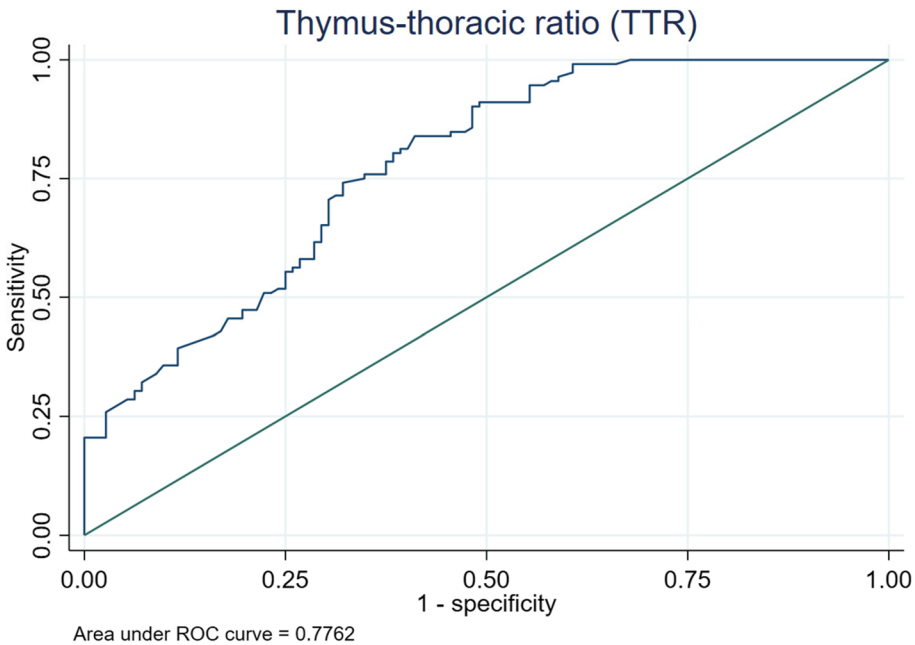

Fig. 1 ROC curve regarding the diagnostic accuracy of thymus size based on the TTR index in diagnosing diabetes in pregnant women

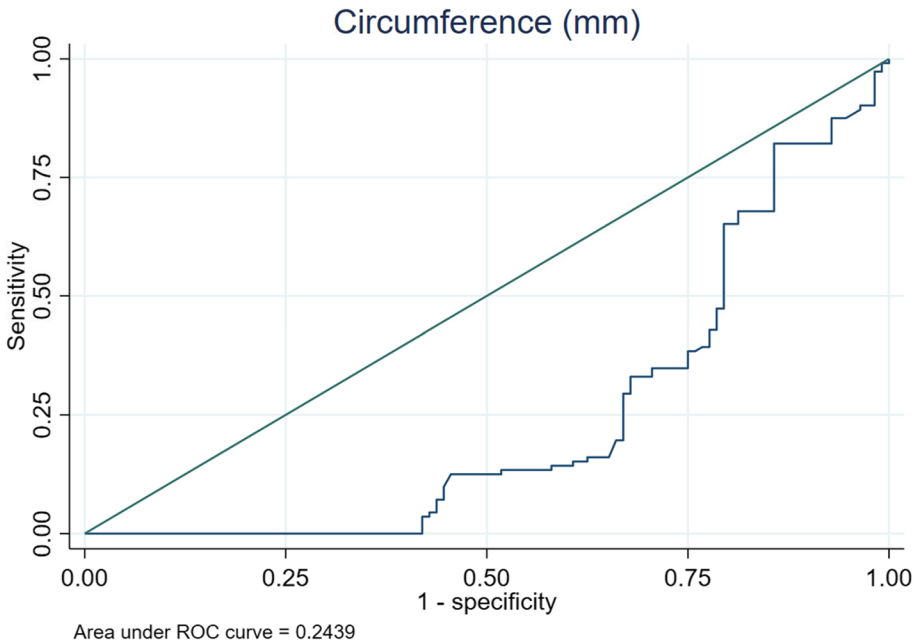

Fig. 2 ROC curve regarding the diagnostic accuracy of thymus size based on the thymus circumference in diagnosing diabetes in pregnant women

circumference in the present study to evaluate fetal thymus size. Based on the results of the present study, it was observed that the TTR index had a higher diagnostic accuracy than the thymus circumference in diagnosing diabetes in pregnant women.

Ghalandarpoor-Attar et al. [24] conducted a study on 160 pregnant women with a case–control design to evaluate the size of the fetal thymus in screening diabetic women. This study used the TTR index to measure thymus size. The results showed a decrease in thymus size in diabetic women compared to the control group. These findings are consistent with the results of the present study. However, their study only used one index to calculate thymus size. Another case–control study involving 320 pregnant women aimed to assess and compare thymus size in diabetic and healthy women. The results of this study, similar to our findings, showed an association between decreased thymus size and the diagnosis of diabetes, with an odds ratio (OR) of 0.69 after controlling for BMI. In other words, diabetic women had a 31% higher chance of reduced thymus size [23]. While our findings are consistent with those of prior research, we believe the novelty of our study lies in its use of both the TTR and thymus circumference as diagnostic measures, comparing their relative effectiveness in diagnosing diabetes in pregnant women.

In the present study, although the relationship between diabetes and thymus size was stronger based on the TTR index, a weak association was also observed based on the thymus circumference index. In the study by Gok et al. [19], a case–control study with 360 samples, the relationship between diabetes and fetal thymus size was assessed. Their results showed no statistically significant association between gestational diabetes and fetal thymus size, contradicting the present study's findings. However, their study used the transverse diameter index to assess thymus size, which may be a possible reason for the discrepancy in results.

Fetal thymus size has been evaluated in various maternal and fetal diseases, and several potential reasons for changes in thymus size have been reported. For example, a decrease in fetal thymus size in women with preterm premature rupture of membranes (PPROM) may be a reliable ultrasound marker for fetal involvement in the systemic inflammatory response [29, 30]. In diabetic women, hypoxia and metabolic stress caused by disturbances in glucose metabolism may be proposed as mechanisms for the decrease in thymus size in the fetus [31]. Based on studies, it appears that increased oxygen consumption due to excess glucose metabolism and the placenta's inability to supply this oxygen due to defects in the structure and function of the placenta in diabetic pregnant women could lead to hypoxic and metabolic stress, subsequently activating the hypothalamic–pituitary–adrenal axis [32].

The limitations of the present study include its retrospective design and the lack of assessment of perinatal outcomes. Additionally, all the samples in this study were

selected from a single healthcare center. The reliance on a single sonographer for all measurements, despite their expertise, may introduce measurement bias and limit the generalizability of our findings. Furthermore, the body mass index (BMI) in this study was calculated and controlled based on the weight and height of pregnant women at the time of hospital admission. The wide range of gestational ages included in this study may introduce variability in thymus size measurements, as thymus development is dynamic and gestational age-dependent. On the other hand, this study did not evaluate the relationship between thymus size and blood glucose levels or maternal hemoglobin A1C levels. Therefore, this association remains unclear at what glucose or hemoglobin A1C level exists. This study utilized the thymic-thoracic ratio (TTR) and thymus circumference for assessing fetal thymus size. While TTR is a widely accepted and reproducible method, and thymus circumference represents a relatively novel approach, we did not employ alternative methods, such as the transverse diameter and perimeter of the thymus, which may provide additional valuable information and improve comparability with other studies. Future research should explore the potential advantages of these newer methods in assessing fetal thymus size and their clinical implications. Despite these contributions, we acknowledge that further research is needed to explore the relationship between thymus size and perinatal outcomes, as our study did not address these factors. Future studies with larger sample sizes, multi-center involvement, and more precise measurements across different stages of pregnancy could provide deeper insights into the role of thymus size in predicting gestational complications and neonatal health outcomes.

Conclusion

The present study suggests that a reduction in fetal thymus size may be associated with diabetes in pregnant women. Moreover, the reduction in thymus size was more pronounced in women with overt diabetes compared to other types of diabetes. Our findings suggest that the thymic-thoracic ratio (TTR) may be a more reliable indicator than thymus circumference for assessing the impact of maternal diabetes on fetal thymus size, although further studies with larger sample sizes and additional predictive analyses are needed to confirm these findings. However, it still needs to be determined whether ultrasound evaluation of fetal thymus size may help predict perinatal outcomes in diabetic women.

Abbreviations

TTR	Thymic-thoracic ratio
BMI	Body mass index
GCT	Glucose challenge test
FBS	Fasting blood sugar
AUC	Area under the curve
PPROM	Premature rupture of membranes
OR	Odds ratio

Acknowledgements

We extend our gratitude to all the women who participated in this study and thank the Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran, for the support, cooperation, and assistance throughout the study (IR.KUMS.MED.REC.1402.090).

Authors' contributions

NM, and NR conceived the project and designed the study. NR, and EKh prepared the data. MB, and AA analyzed the data. MB, EKh, and AA drafted the first version of the manuscript. NM, and AA supervising the project and securing funding. All authors participated in interpreting the data and revising the manuscript. All authors read and approved the final manuscript.

Funding

Any funding resource did not fund this study.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted by the Declaration of Helsinki, and the study was approved by the Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran, with the ethical code IR.KUMS.MED.REC.1402.090. Written informed consent was obtained from all participants before the start of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 31 December 2024 Accepted: 12 March 2025
Published online: 21 March 2025

References

1. Sweeting A, Hannah W, Backman H, Catalano P, Feghali M, Herman WH, et al. Epidemiology and management of gestational diabetes. Lancet. 2024;404(10448):175–92.
2. Perovic M, Gojnic M, Arsic B, Pantic I, Stefanovic T, Kovacevic G, et al. Relationship between mid-trimester ultrasound fetal liver length measurements and gestational diabetes mellitus. J Diabetes. 2015;7(4):497–505.
3. Behboudi-Gandevani S, Amiri M, Bidhendi Yarandi R, Ramezani TF. The impact of diagnostic criteria for gestational diabetes on its prevalence: a systematic review and meta-analysis. Diabetol Metab Syndr. 2019;11:1–18.
4. Sandsæter HL, Horn J, Rich-Edwards JW, Haugdahl HS. Preeclampsia, gestational diabetes and later risk of cardiovascular disease: women's experiences and motivation for lifestyle changes explored in focus group interviews. BMC Pregnancy Childbirth. 2019;19:1–10.
5. Wang J, Chen K, Jin X, Li X, An P, Yang N, et al. Prognostic factors for cesarean section outcome of pregnant women with gestational diabetes mellitus: a systematic review and meta-analysis. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2019;12:913–29.
6. Fuka F, Osuagwu UL, Agho K, Gyaneshwar R, Naidu S, Fong J, et al. Factors associated with macrosomia, hypoglycaemia and low Apgar score among Fijian women with gestational diabetes mellitus. BMC Pregnancy Childbirth. 2020;20:1–14.
7. Nakshine VS, Jogdand SD. A comprehensive review of gestational diabetes mellitus: impacts on maternal health, fetal development,

childhood outcomes, and long-term treatment strategies. Cureus. 2023;15(10):e47500.
8. Shrivastava V, Lee M, Lee D, Pretorius M, Radford B, Makkar G, et al. Beta cell adaptation to pregnancy requires prolactin action on both beta and non-beta cells. Sci Rep. 2021;11(1):10372.
9. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. Int J Mol Sci. 2018;19(11):3342.
10. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational diabetes mellitus: mechanisms, treatment, and complications. Trends Endocrinol Metab. 2018;29(11):743–54.
11. Giannakou K, Evangelou E, Yiallouros P, Christophi CA, Middleton N, Papatheodorou E, et al. Risk factors for gestational diabetes: an umbrella review of meta-analyses of observational studies. PLoS One. 2019;14(4):e0215372.
12. Ghasemi V, Banaei M, Kiani Z, Ramezani Tehrani F, Saei Ghare Naz M. Blood cells parameters in second trimester of pregnancy and gestational diabetes mellitus: a systematic review and meta-analysis. Endocrinology, diabetes, metabolism. 2025;8(1):e70024.
13. Vinnars M-T, Bixo M, Damdimopoulou P. Pregnancy-related maternal physiological adaptations and fetal chemical exposure. Molecular and Cellular Endocrinology. 2023:112064.
14. Ruiz Pérez M, Vandenabeele P, Tougaard P. The thymus road to a T cell: migration, selection, and atrophy. Front Immunol. 2024;15:1443910.
15. Nevo S, Frenkel N, Kadouri N, Gome T, Rosenthal N, Givony T, et al. Tuft cells and fibroblasts promote thymus regeneration through ilc2-mediated type 2 immune response. Sci Immunol. 2024;9(91):eabq6930.
16. Myers R, Hutter J, Matthew J, Zhang T, Uus A, Lloyd D, et al. Assessment of the fetal thymus gland: comparing MRI-acquired thymus volumes with 2D ultrasound measurements. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2021;264:1–7.
17. Caissutti C, Familiari A, Khalil A, Flacco ME, Manzoli L, Scambia G, et al. Small fetal thymus and adverse obstetrical outcome: a systematic review and a meta-analysis. Acta Obstet Gynecol Scand. 2018;97(2):111–21.
18. Erol SA, Kulhan NG, Günenc O. Evaluation of fetal thymus size in pregnancies complicated with fetal growth restriction. Jinekoloji-Obstetrik ve Neonatoloji Tıp Dergisi. 2023;20(1):1617–24.
19. Karaşin SS, Akselim B, Tosun Ö, Karaşin ZT. Decreased fetal thymus size at 24 weeks gestation by ultrasound measurement in gestational diabetes mellitus fetal thymus examination for diabetes. Journal of Obstetrics and Gynaecology Research. 2022;48(6):1348–54.
20. Sinaci S, Sahin D. Can diabetes influence fetal thymus size during pregnancy? Journal of Obstetrics and Gynaecology Research. 2023;49(6):1491–7.
21. Gök K, Özden S. Finding the best method for screening for gestational diabetes mellitus: fetal thymic-thoracic ratio or fetal thymus transverse diameter. Rev Assoc Med Bras. 2023;69:303–7.
22. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes—2025. Diabetes Care. 2025;48(Supplement_1):S27–49.
23. Dörnemann R, Koch R, Möllmann U, Falkenberg MK, Möllers M, Klockenbusch W, et al. Fetal thymus size in pregnant women with diabetic diseases. J Perinat Med. 2017;45(5):595–601.
24. Ghalandarpoor-Attar SN, Borna S, Ghalandarpoor-Attar SM, Hantoushzadeh S, Khezerdoost S, Ghotbizadeh F. Measuring fetal thymus size: a new method for diabetes screening in pregnancy. J Matern Fetal Neonatal Med. 2020;33(7):1157–61.
25. Tangshewinsirikul C, Panburana P. Sonographic measurement of fetal thymus size in uncomplicated singleton pregnancies. J Clin Ultrasound. 2017;45(3):150–9.
26. Kim JM, Oelmeier K, Braun J, Hammer K, Steinhard J, Köster HA, et al. Fetal thymus size at 19–22 weeks of gestation: a possible marker for the prediction of low birth weight? Fetal Diagn Ther. 2024;51(1):7–15.
27. Yildirim M, Oluklu D, Menekse Beser D, Uyan Hendem D, Kara O, Tanacan A, et al. Assessment of fetal thymus size in pregnant women with rheumatic diseases: a case–control study. J Clin Ultrasound. 2023;51(8):1342–7.
28. Zych-Krekora K, Grzesiak M, Kaczmarek P, Perlman S, Bardin R, Gilboa Y, et al. Assessment of fetal thymus size and BMI in pregnant women with diabetes. Ginekol Pol. 2023;94(4):309–14.
29. Kacerovsky M, Matulova J, Andrys C, Mls J, Hornychova H, Kukla R, et al. Preterm prelabor rupture of membranes without microbial invasion of the amniotic cavity and intra-amniotic inflammation: a heterogeneous group with differences in adverse outcomes. J Matern Fetal Neonatal Med. 2022;35(25):9145–56.
30. Menon R. Fetal inflammatory response at the fetomaternal interface: a requirement for labor at term and preterm. Immunol Rev. 2022;308(1):149–67.
31. McElwain CJ, McCarthy FP, McCarthy CM. Gestational diabetes mellitus and maternal immune dysregulation: what we know so far. Int J Mol Sci. 2021;22(8):4261.
32. Gök K, Ozden S. Decreased fetal thymus size in pregnancies after assisted reproductive technologies. J Matern Fetal Neonatal Med. 2023;36(1):2166401.

Publisher's Note