# Comparison of Fetal Thymus Size between Pregnant Women with Diabetic and Non-Diabetic Disease

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## Abstract

**Objective:** To compare fetal thymus size between fetuses of diabetic and non-diabetic pregnant women and to explore the relationship between thymus size, maternal diabetes type, glycemic control, and pregnancy outcomes.

**Materials and Methods:** This prospective study at Bhumibol Adulyadej Hospital included singleton pregnancies between 28 and 34 weeks, with participants divided into control (118 participants) and diabetic (121) groups. Fetal thymic diameter (TD) and thymic thoracic ratio (TTR) were measured via ultrasound. The diabetic group was further classified into pregestational diabetes mellitus (PGDM), GDMA1, and GDMA2. Maternal blood sugar control and HbA1c levels were recorded. Pairwise comparisons with Bonferroni correction identified differences between diabetes types, and receiver operating characteristic (ROC) curve analysis determined the cutoff for fetal thymus size.

**Results:** Among 239 participants, fetuses in the diabetic group had significantly smaller thymus sizes compared to the control group (TD: 32.7 vs. 33.9 mm, TTR: 0.34 vs. 0.40, $p<0.05$). The TTR was significantly lower in PGDM and GDMA2 subgroups than in non-diabetic pregnancies. Poor glycemic control and HbA1c ≥7% was associated with a significantly lower TTR but not TD. ROC analysis identified a TTR cutoff of ≤0.34 (AUC 71%) as a better predictor of fetal thymic size reduction than TD (AUC 58%). Neonatal complications, including higher birth weight, NICU admission, and early neonatal jaundice, were more prevalent in the diabetic group.

**Conclusion:** Fetal thymus size in pregnant women was significantly smaller than that of non-diabetic pregnant women. TTR was an effective measurement to detect the decrease in fetal thymus size.

**Keywords:** Fetal thymus gland; Thymic diameter; Thymic thoracic ratio; Diabetes mellitus; Pregnancy

Received 17 April 2025 | Revised 20 March 2026 | Accepted 23 March 2026

**J Med Assoc Thai 2026;109(6):505-12**

https://doi.org/10.35755/jmedassocthai.2026.6.03010

Diabetes mellitus (DM) is now a significant contributor to the increasing morbidity, mortality, and healthcare costs globally[1]. According to the World Health Organization (WHO), the incidence of DM has been alarmingly increasing from 2000 to 2019. Gestational diabetes mellitus (GDM) is a common health issue among pregnant women. It is also a common problem in Thai pregnant women, where its prevalence was 29.2%[2]. Elevated blood sugar levels in pregnant women, whether pre-existing or identified during pregnancy, directly impact the health of the fetus, leading to conditions such as fetal macrosomia and fetal growth restriction[1].

In the developing fetus, the thymus gland originates from the third brachial cleft and migrates downward to the thoracic area by the 12th week of pregnancy. It completes its development between the 16th and 20th weeks. The thymus gland is typically

**What is already known about this topic?**

DM is a common condition that can impact the growth and development of various organs in the fetus. This study demonstrates that maternal diabetes leads to a reduction in the size of the fetal thymus. When analyzing the effects based on the type of DM, it was found that PGDM had the most significant impact on the size of the fetal thymus. Furthermore, maternal blood sugar control also contributed to a reduction in the size of the fetal thymus.

**What does this study add?**

Measuring fetal thymus size using the TTR is more reliable than using the TD. Our findings suggest that a fetal TTR of less than 0.34 may serve as an indicator of diabetes during pregnancy. In cases of poor blood sugar control or an HbA1c level of ≥7% in pregnant women with diabetes, a reduction in fetal TTR is observed.

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**How to cite this article:**

Supattanarungsi W, Pleankong M, Luangdansakul W, Smanchat B, Bhamarapravatana K, Suwannarurk K. Comparison of Fetal Thymus Size between Pregnant Women with Diabetic and Non-Diabetic Disease. J Med Assoc Thai 2026;109:505-12.

located in the mediastinum anterior to the great arteries and superior vena cava. Its size increases throughout pregnancy[3]. The crucial role of the fetal thymus gland was an immunological function against inflammation and infection.

Maternal glucose metabolism disorders can impact fetal stress and metabolism. Numerous studies were set out to explore the relationship between fetal thymus size and maternal conditions[4]. In recent studies, Kleemann et al. reported that fetal thymus size in Trisomy 13 and 18 pregnancies was smaller than normal[4]. Kim et al. found that a small fetal thymus was associated with newborns below the 10th percentile birth weight[5]. Ghalandarpoor-Attar et al. revealed that fetal thymus size in diabetic pregnant women was smaller compared to those without DM, correlating with adverse pregnancy outcomes[6]. Sinaci & Sahin similarly found smaller thymus sizes in fetuses of diabetic pregnant women versus non-diabetic counterparts[7]. However, there was no conclusion on the exact relationship between the size of the fetal thymus gland and peripartum conditions such as preterm birth, chorioamnionitis, neonatal sepsis, and overall morbidity[8,9].

Various ultrasonographic methods have been used to measure fetal thymus size, including transverse diameter, anterior-to-posterior diameter, circumference, volume, thymic head circumference ratio (THR), and thymic thoracic ratio (TTR)[10-12]. Many studies focused on these ratios due to their accessibility and stability during pregnancy in normal fetuses[9,10].

This study aimed to compare the thymus gland size between fetuses of diabetic and non-diabetic pregnant women. It is also a seeker to investigate the relationship between fetal thymus size, the type of maternal diabetes, and maternal glucose control. Additionally, correlations between fetal thymus size and pregnancy, as well as neonatal outcomes, would be explored.

## Materials and Methods

This prospective analytical study was conducted in the Department of Gynecology and Obstetrics at Bhumibol Adulyadej Hospital (BAH), Bangkok, Thailand. Ethical approval was obtained from the Institutional Review Board of BAH on March 18, 2024 (IRB No. 19/67). The clinical trial registered number was TCTR20240418005. Pregnant women with singletons between 28 and 34 weeks of gestation who visited the antenatal care (ANC) clinic for fetal growth estimation by ultrasonography between April 1 and December 31, 2024, were recruited. The exclusion criteria were women with any known medical diseases (chronic hypertension, cardiovascular disease, liver disease, chronic kidney disease, inflammatory bowel disease, and autoimmune connective tissue diseases). Moreover, HIV infection, substances used, smoking, and fetal structural or chromosomal abnormalities were also excluded. Out of those visiting our facility, 244 participants were recruited. Those participants signed the consent forms.

Recruited participants were divided into two groups: diabetic [including pregestational diabetes mellitus (PGDM), GDM with diet control and lifestyle modifications (GDMA1), and GDM with medication therapy (GDMA2)] and non-diabetic groups. The non-diabetic groups were the pregnant women who had been appointed to the ANC clinic with similar demographic and clinical characters. Each group had 122 participants. At their first visits, all pregnant women underwent screening tests, namely fasting blood sugar (FBS), HbA1c, and random blood sugar tests to detect glucose metabolism abnormalities. Further evaluation was conducted if abnormal results indicated PGDM (FBS >126 mg/dL, HbA1c ≥6.5%, or random BS >200 mg/dL). For patients with normal initial results, universal screening with a 75g oral glucose tolerance test (OGTT) was scheduled between 24 and 28 weeks of gestation. GDM was diagnosed if patients' plasma glucose values equaled or exceeded the following thresholds: fasting 92 mg/dL, 1-hour 180 mg/dL, 2-hour 153 mg/dL according to the Carpenter criteria[1]. Patients diagnosed with GDM who could manage their condition through diet and lifestyle modifications without requiring medication were classified as GDMA1. GDMA2 referred to patients who required medication to control their blood sugar levels[1]. Baseline characteristic data were recorded in this study, including maternal age, body mass index (BMI), and gestational age at ultrasound scanning. A flow chart of the study is shown in Figure 1.

Participants underwent routine ultrasonographic studies to estimate fetal weight, conduct anomaly scans, determine placental location, and assess amniotic fluid volume. Measurements of fetal thymic diameter (TD) and TTR were taken three times for both groups by attending physicians and fellows at the MFM unit using a Voluson (E6, E8, E10) ultrasound machine from GE Healthcare, USA, with an RAB 4-8 L probe. The mean values were recorded using the Viewpoint 6 program (Version 6.11, GE Healthcare, USA).

From the pilot study, the mean and standard deviation of thymic size in the study and control groups were 32.5±3.2 and 34.1±4.1, respectively. The alpha

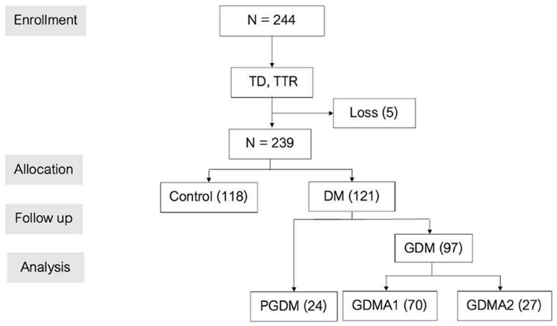


**Figure 1.** Flow of the study.

TD, thymic diameter; TTR, thymic thoracic ratio; Loss, loss to follow up due to delivery at other hospital; DM, diabetes mellitus; GDM, gestational diabetes mellitus, GDMA1, GDM with diet control and lifestyle modifications; GDMA2, GDM with medication therapy; PGDM, pregestational diabetes mellitus

and beta errors were set at 0.05 and 0.1, respectively. The minimum sample size was 111 cases for each group. An additional 10% was added to account for potential attrition. Finally, 122 cases were recruited for each group.

The technique for measuring fetal TD and TTR was standardized, adopted from Cho et al.[10] and Chaoui et al[13]. Figure 2 illustrates the measurement process. Initially, the four-chamber views in the axial plane of the thorax were identified. The image was then cranially scrolled to display the three-vessel view (3VV) and magnified to occupy more than 50% of the display. The thymus, located anterior to the pulmonary artery, aorta, and superior vena cava, and positioned between both lungs laterally, was identified. Subsequently, digital markers (2-point function) were employed to draw a line between the two lateral edges of the thymus at its greatest width to measure TD. Finally, in the same plane, the TTR was computed by dividing the distance from the sternum to the posterior border of the thymus by the distance from the sternum to the spine.

Obstetric and neonatal outcomes were collected for further analysis. Self-monitoring blood glucose level, HbA1c, pregnancy induce hypertension (PIH), gestational age at delivery, fetal gender, fetal birth weight, rate of cesarean section, birth asphyxia (Apgar score at 1 minute <7), length of hospital stays (LOS), neonatal intensive care unit (NICU) admission, and early neonatal jaundice were all recorded. Data analysis was performed using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA). Baseline characteristics were described as mean ± standard deviation or number (%). Independent t-test and chi-square test were used to assess continuous and categorical variables, respectively. One-way ANOVA with Bonferroni post hoc tests was used to compare multiple groups. A p-value less than 0.05 was considered statistically significant.

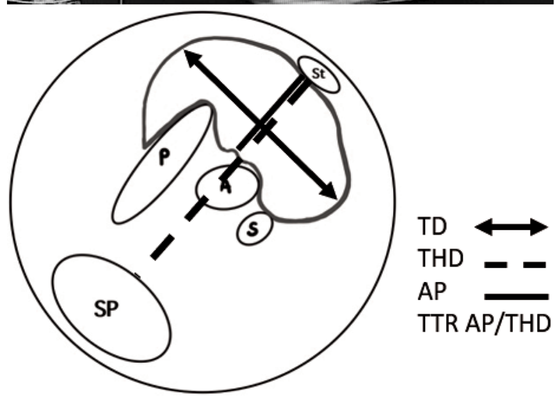


**Figure 2.** Ultrasonography image demonstrating the measurement of TD and TTR.

Note: Ultrasonography display shows the three-vessel view (3VV)
P, pulmonary artery; A, aorta; S, superior vena cava; SP, spine; St, sternum; TD, thymic diameter; THD, thoracic diameter; AP, anteroposterior diameter; TTR, thymic thoracic ratio

## Results

A total of 244 participants were initially enrolled in the study. Ultrasound scanning was done in 122 participants in the study group and 122 participants in the control group. During the follow-up period, five patients were lost to follow-up due to delivery at their urban residences, as shown in Figure 1. The study group (121 participants) and the control group (118) were analyzed. The baseline characteristics of participants in both groups are summarized in Table 1. Fetal birth weight, preterm delivery, the incidence of cesarean section, rates of NICU admission, LOS, and early neonatal jaundice in the study group were significantly higher than in the

**Table 1.** Comparison of baseline and clinical characters and fetal thymus size (TD, TTR) between diabetic (study, n=121) and non-diabetic (control, n=118) pregnant women

| | Study | Control | p-value |
|---|---|---|---|
| Age (years); mean±SD | 33±5.2 | 31.8±5.9 | 0.100 |
| BMI (kg/m$^2$); mean±SD | 27.2±5.3 | 25.7±4.3 | 0.254 |
| GA at study (weeks); mean±SD | 31.9±1.5 | 31.8±1.4 | 0.458 |
| SMBG; n (%) | | | |
| Well control | 86 (71.1) | - | N/A |
| Poor control | 35 (28.9) | - | N/A |
| HbA1c; n (%) | | | |
| ≥7 | 12 (9.9) | - | N/A |
| <7 | 16 (13.2) | - | N/A |
| GA at delivery (weeks); mean±SD | 38.3±1.1 | 38.9±1.1 | <0.001 |
| PIH; n (%) | 7 (5.8) | 6 (5.1) | 0.741 |
| Cesarean delivery; n (%) | 60 (49.6) | 27 (22.9) | <0.001 |
| Female; n (%) | 60 (49.6) | 59 (50) | 0.949 |
| Birth weight (kg); mean±SD | 3.2±0.5 | 3.0±0.3 | 0.008 |
| Apgar at 1 minute; mean±SD | 8.9±0.6 | 8.9±0.3 | 0.420 |
| Apgar at 5 minutes; mean±SD | 9.88±0.2 | 9.9±0.2 | 0.685 |
| Preterm delivery; n (%) | 8 (6.6) | 2 (1.7) | 0.058 |
| Length of stay (days); mean±SD | 2.9±1.9 | 2.2±0.5 | <0.001 |
| NICU admission; n (%) | 6 (5) | 0 (0) | 0.014 |
| Early neonatal jaundice; n (%) | 16 (13.2) | 4 (3.4) | 0.006 |
| TD (mm); mean±SD | 32.7±4.4 | 33.9±4.0 | 0.025 |
| TTR; mean±SD | 0.34±0.05 | 0.40±0.06 | <0.001 |

SD=standard deviation; BMI=body mass index; GA=gestational age; SMBG=self-monitoring blood glucose; HbA1c=glycated hemoglobin; PIH=pregnancy induce hypertension; NICU=neonatal intensive care unit; TD=thymic diameter; TTR=thymic thoracic ratio; N/A=not applicable

control group (Table 1). Additionally, the study group had a gestational age at delivery less than the control group (38.31 vs. 38.93 weeks, $p<0.001$). Other factors, including mean maternal age, BMI, gestational age at the time of data collection, PIH, fetal gender, and Apgar at one min were comparable between the two groups. Two-thirds of pregnant mothers in the study group (86/121) achieved well-controlled blood glucose. Notably, the thymus gland of fetuses with diabetic mothers was smaller than that of the control group with statistical significance (TD: 32.7 vs. 33.9 mm, TTR: 0.34 vs. 0.40, respectively, $p<0.05$). There were 4 cases of early neonatal sepsis in the study group that needed empirical antibiotic treatment.

In the subgroup analysis based on the type of DM, TTR was significantly lower in the GDMA2 and PGDM groups compared to those in the control group, as shown in Figure 3. Figure 4 and 5 illustrated that the group with poorly controlled glucose and HbA1c ≥7% exhibited significantly lower TTR values compared to the well-controlled group and those with HbA1c <7%. However, no significant difference in TD was observed between the two groups.

In the present study, we identified the optimal cutoff values for TD and TTR in pregnancies complicated by diabetes using receiver operating characteristic (ROC) curve analysis. For TD, the optimal cutoff was determined to be ≤30.55 mm, which yielded a sensitivity of 38%, a specificity of 83.9%, and an overall accuracy of 60.7%. An area under the curve (AUC) for TD was 58%. In contrast, the TTR cutoff of ≤0.34 demonstrated significantly higher performance (AUC 71%), with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy at 57.9%, 78.8%, 73.7%, 64.6%, and 68.2%, respectively. Furthermore, the Youden Index for TTR was 0.367, reflecting its superior discriminatory power compared to TD (Table 2).

## Discussion

This prospective study was conducted to compare fetal thymus size between those belonged to diabetes and non-diabetes pregnant women. Demographic characteristics, namely maternal age, BMI, and gestational age at study, of both groups were comparable. However, fetuses in the study group had higher average birth weight, cesarean delivery rate, longer LOS, and more neonatal complications, such as NICU admissions and early neonatal jaundice, than the control group. The average gestational age at delivery of the study group was less than that of the control group (38.3 and 38.9 weeks) without statistical significance. One-third (35/121) of the study group had poor glycemic control. This finding might be the explanation for why neonatal complications, including higher birth weight, longer LOS, NICU admission, and early neonatal jaundice, were more prevalent in the study group than in the control group. These findings were not unexpected, as diabetes had been known to elevate the risk of complications for both the mother and the fetus[14].

From the current study, TD and TTR in the study group were significantly lower than those of the control group, as shown in Table 1. When subgroup analysis of the study group, namely GDMA1, GDMA2, and PGDM, was compared to the control group, TD between subgroups were not statistically significantly different as shown in Figure 3. In contrast, regarding TTR and subgroup analysis, TTR in the control group was significantly higher than in GDMA2 and PGDM ($p<0.001$), as presented in Figure 3. This finding indicated that TTR was an appropriate indicator for determining the fetal thymus size in GDM pregnant

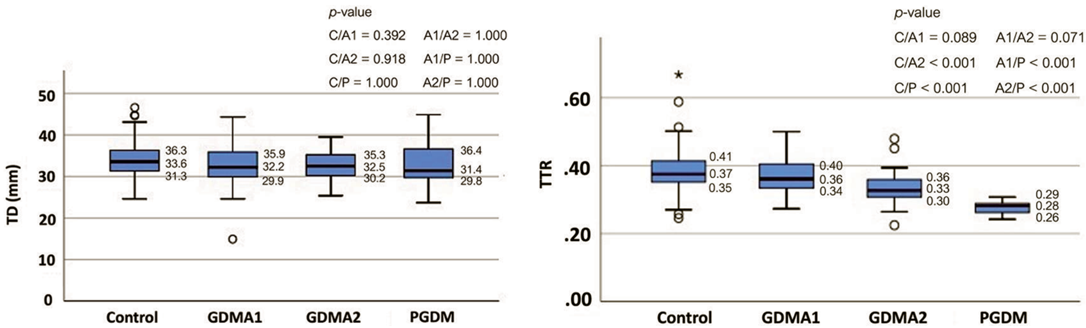


**Figure 4.** Comparison of TD and TTR between well control and poor control glucose level groups.

Note: Well control: >70% of SMBG values within target range per patient, Poor control: <70% of SMBG values within target range per patient
TD, thymic diameter; TTR, thymic thoracic ratio, SMBG, self-monitoring blood glucose

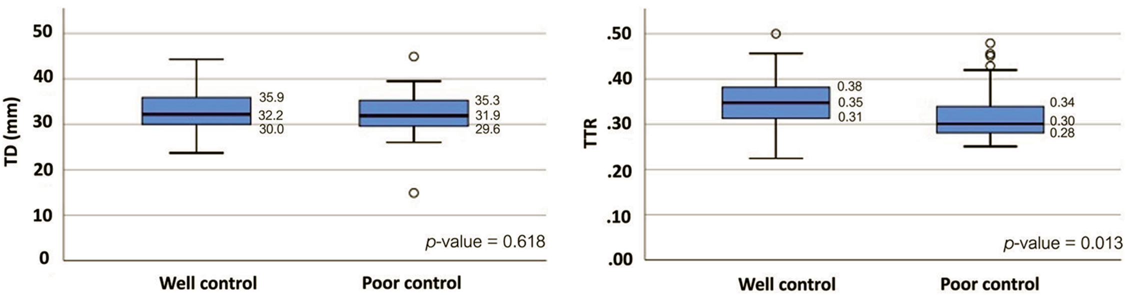


**Figure 5.** Comparison of TD and TTR between groups with HbA1c ≥7% and HbA1c <7%.

Note: HbA1c was collected at the first ANC visit in pregnant women with diabetes
TD, thymic diameter; TTR, thymic thoracic ratio; HbA1c, glycated hemoglobin

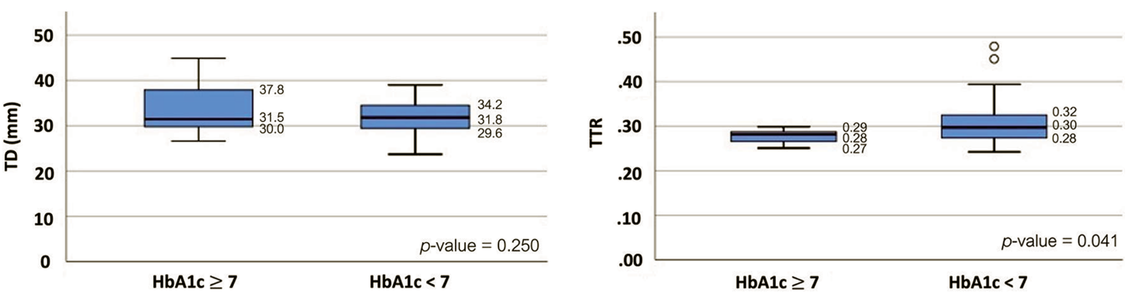


**Figure 3.** Comparison of TD and TTR between control and diabetes type groups.

Note: GDMA1: diabetes patients who required diet control to manage their blood sugar levels, GDMA2: diabetes patients who required medication to manage their blood sugar levels

TD, thymic diameter; TTR, thymic thoracic ratio; GDM, gestational diabetes mellitus; PGDM, pregestational diabetes mellitus; C, control group; A1, GDMA1 group; A2, GDMA2 group; P, PGDM group; C/A1, control to GDMA1 group ratio; C/A2, control to GDMA2 group ratio; C/P, control to PGDM group ratio; A1/A2, GDMA1 to GDMA2 group ratio; A1/P, GDMA1 to PGDM group ratio; A2/P, GDMA2 to PGDM group ratio

**Table 2.** ROC curve of TD and TTR in diabetes pregnancy

| | AUC (95% CI) | Cut-off | Sensitivity | Specificity | PPV | NPV | Accuracy | Youden index |
|---|---|---|---|---|---|---|---|---|
| TD | 0.58 (0.508 to 0.653) | ≤30.55 | 38% | 83.9% | 70.8% | 56.9% | 60.7% | 0.219 |
| TTR | 0.71 (0.649 to 0.780) | ≤0.34 | 57.9% | 78.8% | 73.7% | 64.6% | 68.2% | 0.367 |

ROC=receiver operating characteristic; AUC=area under curve; PPV=positive predictive value; NPV=negative predictive value; CI=confidence interval; TD=thymic diameter; TTR=thymic thoracic ratio women with GDM. The reason why TTR did not show a statistically significant difference between the control and GDMA1 groups was that GDMA1 represented a mild degree of GDM. The high maternal blood sugar might be affecting fetal thymus size[15,16]. Further analysis of TD and TTR between participants with well-controlled and poorly controlled glucose levels in the study group showed that only TTR in the poorly controlled glucose level group was lower than that in the well-controlled group, with statistical significance, as shown in Figure 4.

Figure 5 showed TD and TTR in high (≥7%) and low (<7%) HbA1c levels patients were evaluated. High HbA1c indicated a poor glycemic control history. TTR of the high HbA1c group was lower than that of the control group with statistical significance (p=0.041). The current study revealed that fetal thymus glands of pregnant mothers with poor glycemic control of diabetes were smaller than those from the control group. High maternal glucose levels were related to the decreasing size of the fetal thymus gland. TTR was an effective and accurate measurement for the evaluation of intrauterine fetal thymus size[13].

Fetal thymus size was associated with gestational age, fetal weight, and maternal stress conditions, including diabetes[17-19]. Pregnant mothers with diabetes had increased cortisol levels. High cortisol affects the hypothalamic-pituitary-adrenal axis, reduces T-cell production in the fetal thymus, and induces thymocyte apoptosis, ultimately leading to a decrease in thymus size[18,19].

There were higher neonatal complications among the study group than in the control group, namely, LOS, NICU admission, and early neonatal jaundice (Table 1). This was the consequence of poor glycemic control, shown in either high postprandial glucose or HbA1c levels in pregnant women.

Small fetal thymus size is a consequence of elevated maternal blood sugar being transferred to the fetus through the placenta. This elevated blood sugar leads to increased insulin production and metabolic activity in the fetus, particularly in the liver, causing greater oxygen consumption. Additionally, maternal hyperglycemia induces oxidative stress and inflammation, which impair placental function and reduce oxygen delivery to the fetus, resulting in fetal hypoxia. The reduced oxygen supply damages thymocytes, leading to thymus involution and a subsequent reduction in thymus size[15,16].

Our finding of a small fetal thymus size among pregnant women with diabetes aligns with results from previous studies by Dörnemann et al., Ghalandarpoor-Attar et al., Gök & Özden, and Sinaci & Sahin[6,7,9,11]. However, the measurement of thymus size using TD in this study did not show significant differences between the control and study groups, which is consistent with Gök & Özden's study from Turkiye in 2023[9]. This might be because the number of mothers with well-controlled blood sugar in this study was similar to that in Gök & Özden's study (71% vs. 58%)[9], and this higher percentage of well-controlled blood glucose levels may have influenced the results compared to other studies.

In contrast to Zych-Krekora et al. and Sinaci & Sahin's studies, TD measurement could be used to detect a small fetal thymus size[7,20]. Well glycemic control patients in the studies by Zych-Krekora et al.[20] and Sinaci & Sahin[7] were lower than in the studies by Gök & Özden[9] and the present research (36%, 41%, 58%, and 71%, respectively)[7,9,20]. This difference can be attributed to the higher levels of maternal blood sugar influencing the reduction in fetal thymus size as measured by TD. TTR from the current study was an effective tool for evaluating small fetal thymus size. The findings of the current work were in line with the work from Dörnemann et al., Ghalandarpoor-Attar et al., Gök & Özden, and Sinaci & Sahin[6,7,9,11]. A comparison of this study to the previous studies was summarized in Table 3.

From Table 2, the TTR ROC curve for the prediction of GDM condition showed an AUC of 71. The appropriate cutoff point of TTR was 0.34. It gave sensitivity, PPV, and NPV at 57.9%, 73.7%, and 64.9%, respectively. Compared to the previous studies of Dörnemann et al. and Gök & Özden, the TTR cut-off point was suggested at 0.33 and 0.407, respectively[9,11]. The sensitivity and specificity from the current study were lower than those found in the studies by Dörnemann et al. and Gök & Özden (57.9/78.8%, 87.6/76.2%, and 92.8/86.1%, respectively)[9,11]. The high percentage of pregnant women with poor glycemic control might have impacted the diagnostic performance. Previous studies with a higher prevalence of poorly controlled blood glucose, smaller fetal thymus sizes are more frequently observed, which can result in better sensitivity and specificity compared to studies with fewer mothers having poorly controlled glucose levels. This study aimed to evaluate the appropriate TTR between pregnant women with diabetes and those with normal pregnancies. TTR was not used to predict GDM in the present study. The time required for the thymic measurement evaluation was approximately 10 minutes per case. We suggest using the thymic measurement in suspected cases. Further studies with a larger sample size are recommended.

**Table 3.** Comparison of the current study with previous literature on fetal thymus size and maternal diabetes

| | Present | Dörnemann[11] | Ghalandarpoor[6] | Gök[9] | Zych-Krekora[20] | Sinaci[7] |
|---|---|---|---|---|---|---|
| Year | 2024 | 2017 | 2020 | 2023 | 2023 | 2023 |
| Country | Thailand | Germany | Iran | Türkiye | Israel | Türkiye |
| Case (n) | 121 | 161 | 80 | 180 | 63 | 105 |
| Population (n) | 239 | 322 | 160 | 360 | 63 | 393 |
| Age (years) | 32.9 | 32.6 | 33.2 | 32 | 33 | 30.9 |
| BMI (kg/m$^2$) | 27.2 | 26.4 | 27.9 | 26.8 | All | 28.5 |
| GAU (weeks) | 28-34 | 19-36 | 19-37 | All | $14^{+5}$-40 | 20-37 |
| DM; n (%) | | | | | | |
| GDMA1 | 70 (57.8) | 29 (18.0) | 20 (25.0) | 106 (58.8) | 23 (36.5) | 40 (38.1) |
| GDMA2 | 27 (22.4) | 69 (42.8) | 31 (38.7) | 74 (41.2) | 29 (46.0) | 42 (40.0) |
| PGDM | 24 (19.8) | 63 (39.2) | 29 (36.2) | - | 11 (17.5) | 23 (21.9) |
| Measurement | | | | | | |
| TD | NS | - | - | NS | S | S |
| TTR | S | S | S | S | - | S |
| WGC | 86/121 | 29/161 | 20/80 | 106/180 | 23/63 | 44/105 |
| Cut-off value | | | | | | |
| TD (mm) | 30.55 | | | | | |
| TTR | 0.34 | 0.33 | | 0.407 | | |
| • Sensitivity (%) | 57.9 | 87.6 | | 92.8 | | |
| • Specificity (%) | 78.8 | 76.2 | | 86.1 | | |

BMI=body mass index; GAU=gestational age at ultrasound; DM=diabetes mellitus; GDM=gestational diabetes mellitus; PGDM=pregestational diabetes mellitus; TD=thymic diameter; TTR=thymic thoracic ratio; NS=no statistically significant; S=statistically significant; WGC=well glycemic control

The strength of the present study was a prospective design and the use of the various parameters to measure fetal thymus size. The authors specifically evaluated the impact of glycemic control on fetal thymus size and followed the participants through to delivery. However, the study has several limitations, including a relatively small sample size, a lack of long-term follow-up on neonatal immunological activity, and potential confounding factors, such as gestational age and fetal weight, that may influence fetal thymus growth.

In conclusion, the current study demonstrated that maternal diabetes, particularly PGDM and poor glycemic control, was associated with small fetal thymus size. The TTR appeared to be a more sensitive tool to reveal the effects of glycemic control, suggesting it could serve as a more accurate tool for assessing these impacts.

## Conclusion

Fetal thymus size in pregnant women was significantly smaller than those from non-diabetes pregnant women. TTR was an effective measurement to detect the fetal thymus size.

## Acknowledgement

The authors would like to sincerely thank the Maternal-Fetal Medicine staff and team at Bhumibol Adulyadej Hospital, Bangkok, Thailand, for their invaluable support in data collection and patient care throughout this study.

## Authors' contributions

WS and MP designed the research, collected, summarized, and analyzed the clinical data, and wrote the manuscript. MP is the corresponding author. KS and KB contributed to data collection, wrote and approved the final manuscript, and provided critical feedback. All authors read and approved the final manuscript. Conceptualization and methodology: WS, MP, WL, and BS. Investigation: WS and MP. Formal analysis: WS, KS, and BS. Visualization and writing-original draft: WS, MP, and KS. Writing-review and editing: WS, MP, KS, and KB. Supervision: MP.

## Clinical trial registration

This study was registered at the Thai Clinical Trials Registry (TCTR) with the registration number TCTR20240418005.

## Conflicts of interest

The authors declare that there are no conflicts of interest.

## Data availability statement

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

## Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok, Thailand (IRB No. 19/67; approved on March 18, 2024). Written informed consent was obtained from all participants prior to enrollment in the study.


## Funding disclosure

This research was supported by the Department of Obstetrics and Gynecology at Bhumibol Adulyadej Hospital.


## Use of artificial intelligence

The authors declare that no artificial intelligence (AI) tools or technologies were used in the design, data collection, analysis, or writing of this manuscript.

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