

# Comparative Analysis of Fetal Brain Structures in Gestational Diabetes versus Normal Pregnancy: A Prospective Cohort Study

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**Objective:** To evaluate whether gestational diabetes mellitus (GDM) affects fetal brain structures, including the cavum septum pellucidum (CSP), posterior lateral ventricle (PLV), cisterna magna (CM), cerebellum, and thalamus by prenatal ultrasound, and to examine the association between maternal hemoglobin A1c (HbA1c) levels and these structures.

**Materials and Methods:** The present study was a prospective cohort study that included 100 singleton pregnancies, which included 50 GDM and 50 non-GDM, at Rajavithi Hospital, Bangkok, Thailand. All participants underwent HbA1c testing and prenatal ultrasound between 29 and 32 weeks of gestation to assess CSP, PLV, CM, cerebellum, and thalamus. Perinatal and neonatal outcomes were subsequently recorded.

**Results:** Baseline demographic characteristics were similar between groups except for higher mean (SD) HbA1c levels in the GDM group at 5.04% (0.44) versus 4.83% (0.40) ( $p=0.018$ ). Among brain structures, only the mean (SD) PLV was significantly larger in the GDM group compared with controls at 5.45 mm (1.25) versus 4.69 mm (1.01) ( $p=0.001$ ). HbA1c levels were positively correlated with the PLV ( $r=0.258$ ,  $p=0.009$ ) and CM ( $r=0.240$ ,  $p=0.016$ ). Receiver operating characteristic (ROC) curve analysis revealed that the PLV exhibited fair discriminative ability in identifying pregnancies with GDM (AUC 0.697,  $p=0.001$ ). Using PLV as a predictor of GDM, a cutoff of 4.6 mm yielded a sensitivity of 74% and specificity of 60%, while a cutoff of 5.0 mm showed lower sensitivity (60%) but higher specificity (74%). Perinatal and neonatal outcomes were similar between groups.

**Conclusion:** Fetuses of mothers with GDM demonstrated significantly larger PLVs, which correlated with maternal HbA1c levels and showed fair discriminative ability for GDM. These findings suggest that maternal glycemic status may influence fetal development of the lateral ventricle and that prenatal ultrasound could serve as a valuable tool for early detection.

**Keywords:** Gestational diabetes mellitus; Fetal brain structures; Cavum septum pellucidum; Lateral ventricle; Cisterna magna

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Gestational diabetes mellitus (GDM) is defined as glucose intolerance first identified during pregnancy. According to the 2024 International Diabetes Federation (IDF) report, GDM affects an estimated 16% of pregnancies worldwide, and its prevalence continues to rise<sup>(1)</sup>. The underlying pathophysiology is linked to placental hormone production, which induces a degree of insulin resistance. In some women, this resistance becomes excessive, leading to GDM<sup>(2)</sup>.

The presence of GDM carries significant implications for both maternal and fetal health. Affected mothers face higher risks of preeclampsia and operative delivery. They are also at increased risk for long-term progression to type 2 diabetes mellitus. For the fetus, GDM is associated with complications such as macrosomia, birth trauma, fetal distress, and intrauterine demise. Furthermore, fetuses exposed to hyperglycemia in utero have an elevated risk of obesity and metabolic disease later in life<sup>(3-5)</sup>.

Emerging evidence from studies in adults with diabetes indicates that the disease is associated with both structural and functional brain alterations. These include reduced volumes of the cerebrum, cerebellum, putamen, and thalamus<sup>(6-10)</sup>. Similarly, studies in neonates and children born to mothers with GDM report effects on brain structure and function. Examples include slight dilatation of the lateral ventricles (LVs) in the neonatal period and poorer neurological development, especially in motor and language domains, compared with offspring

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of non-diabetic mothers<sup>(3,11,12)</sup>. The underlying pathogenesis remains incompletely understood. It is thought to involve complex interactions among hyperglycemia, oxidative stress, inflammation, altered gene expression, and disruptions in cellular and molecular processes<sup>(13)</sup>.

Most prior studies have investigated the effects of maternal diabetes on brain development in neonates or children, while data from the prenatal period remain limited<sup>(14-16)</sup>. Therefore, the authors aimed to examine the impact of GDM on fetal brain structures by routine ultrasound, comparing fetuses of mothers with GDM to those of non-diabetic mothers, to determine whether fetal structural brain differences can be detected during pregnancy.

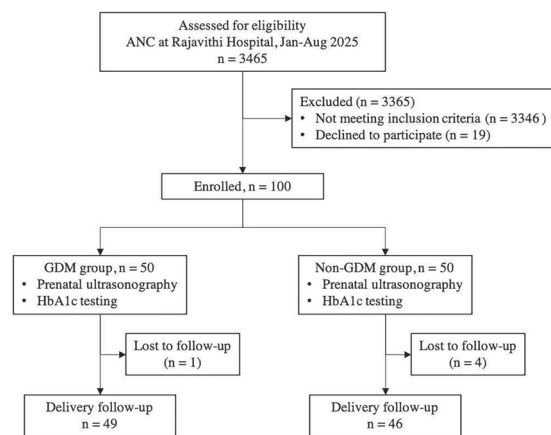
## MATERIALS AND METHODS

The present study was a prospective cohort study conducted at Rajavithi Hospital, Bangkok, Thailand, between January 7, 2025, and August 30, 2025. One hundred singleton pregnant women at 29 to 32 weeks of gestation were enrolled, comprising 50 pregnancies complicated by GDM and 50 without GDM (Figure 1). All participants underwent hemoglobin A1c (HbA1c) testing and prenatal ultrasound at 29 to 32 weeks of gestation to measure the widths of the cavum septum pellucidum (CSP), posterior lateral ventricle (PLV), cisterna magna (CM), trans cerebellar diameter (TCD), and thalamus. Perinatal and neonatal outcomes were subsequently recorded.

The present study aimed to evaluate whether GDM affected fetal brain structures using routine prenatal ultrasound. It also examined the association between maternal HbA1c levels, a marker of average blood sugar levels, and these brain structures. The study protocol was approved by the Institutional Review Board of Rajavithi Hospital (approval No. 67232). Written informed consent was obtained from all participants before enrollment.

The authors estimated the required sample size using the formula for comparing the means of two independent groups<sup>(17)</sup>, based on reported mean (standard deviation, SD) widths of the CSP by Ruth Gründahl et al.<sup>(14)</sup>: 5.0 mm (1.1) in the GDM group and 4.3 mm (1.0) in non-diabetic pregnancies. Using a power of 80% and a significance level of 0.05, the authors calculated that a minimum of 36 participants was required per group. Allowing for a 20% dropout rate, the final required sample size was 50 participants per group, resulting in 100 participants.

Exclusion criteria included women with pregestational diabetes or those diagnosed with

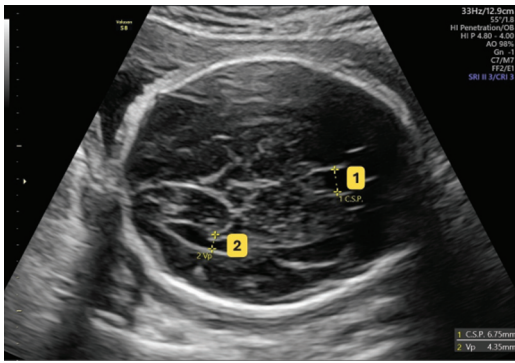


**Figure 1.** Flow diagram of participant enrollment and allocation in the present study.

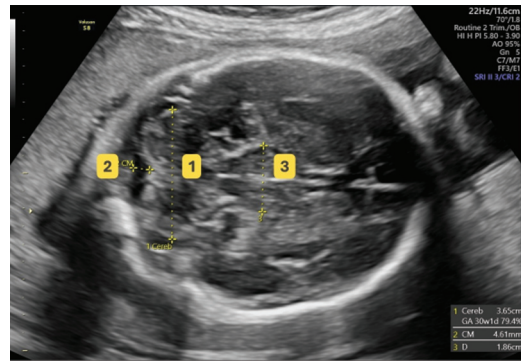
GDM after 32 weeks of gestation. Also excluded were women with significant fetal abnormalities, brain anomalies, or abnormal head shapes, such as dolichocephaly, with a cephalic index of less than 74, brachycephaly with a cephalic index greater than 84, microcephaly, with a head circumference of less than 3 SD, or macrocephaly with a head circumference greater than +2 SD. Fetuses with chromosomal abnormalities or fetal growth restriction with an estimated fetal weight of less than the tenth percentile were also excluded. Additional exclusions were maternal systemic comorbidities, including chronic hypertension, systemic lupus erythematosus, antiphospholipid syndrome, renal disease, or heart disease.

Gestational age in the control group was matched to that of women with GDM at enrollment. GDM was diagnosed using the standard two-step method. Participants first underwent a 50 g glucose challenge test. Those with plasma glucose levels at or above 140 mg/dL proceeded to a 100 g, 3-hour oral glucose tolerance test (OGTT) after an overnight fast. Blood samples were collected at fasting, 1, 2, and 3 hours. GDM was diagnosed according to the Carpenter and Coustan criteria if at least two values met or exceeded the threshold.

Management of GDM consisted of lifestyle modification, including nutritional counseling, dietary adjustment, and regular physical activity. Women were advised to perform self-monitoring of fasting and postprandial blood glucose to maintain optimal glycemic control. Target levels were defined as fasting plasma glucose between 70 and 95 mg/dL. Either a 1-hour postprandial target of 110 to 140 mg/dL or a 2-hour postprandial target of 100 to 120



**Figure 2.** Transventricular plane of the fetal brain demonstrating measurement of the cavum septum pellucidum (CSP, label 1) and the posterior lateral ventricle (PLV, label 2), performed according to ISUOG guidelines<sup>(19)</sup>.



**Figure 3.** Transcerebellar plane of the fetal brain demonstrating measurements of the transcerebellar diameter (TCD, label 1), cisterna magna (CM, label 2), and transverse thalamic diameter (label 3), performed according to ISUOG guidelines<sup>(19)</sup>.

mg/dL was also used as a target. Medical therapy was initiated if more than 30% of glucose readings remained above target despite dietary intervention<sup>(18)</sup>.

Maternal demographic data, OGTT results, and HbA1c levels were recorded. Fetal biometry, amniotic fluid volume, and intracranial structures were assessed by ultrasonography between 29 and 32 weeks of gestation. Intracranial measurements included the PLV, CSP, CM, TCD, and thalamus. Fetuses were considered abnormal and excluded if the PLV was 10 mm or more, CM was less than 2 mm or more than 10 mm, or TCD or thalamic diameter was below the fifth percentile or above the ninety-fifth percentile. Perinatal and neonatal outcomes were recorded for all participants, including gestational age at delivery, mode of delivery, birth weight, Apgar score, and neonatal complications.

Ultrasound examinations were performed using the GE Voluson S8 by a single operator, in accordance with International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines<sup>(19)</sup>. The transventricular plane assessed the LVs and CSP. The PLV was measured at the atrium, with calipers placed on the inner edges of the ventricular walls, perpendicular to the long axis. The CSP width was measured from the inner edge to the inner edge across the midline (Figure 2). The transcerebellar plane, obtained by slight posterior tilting, visualized the thalamus, cerebellum, and CM. The TCD was measured between the outer cerebellar margins; the transverse thalamic diameter at the thalamus's widest points; and the CM as the distance from the posterior vermis to the inner occipital bone (Figure 3).

Descriptive statistics were presented as mean (SD) for continuous variables and as a number (percentage) for categorical variables. Comparisons

between the GDM and non-GDM groups were performed using the independent t-test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Correlations between maternal HbA1c levels and fetal brain measurements for CSP, PLV, CM, TCD, and thalamus were assessed using Pearson's correlation coefficient. Receiver operating characteristic (ROC) curve analysis was applied to evaluate the discriminative performance of fetal brain structures for identifying GDM and to determine optimal cutoff values using Youden's index. Statistical significance was defined as a p-value of less than 0.05. Analyses were conducted using Stata Statistical Software, version 18 (StataCorp LLC, College Station, TX, USA).

## RESULTS

One hundred singleton pregnancies involving 50 GDM and 50 non-GDM were included. Baseline maternal demographic and clinical characteristics were comparable between groups (Table 1). Specifically, there were no significant differences in maternal age, nationality, parity, or pre-pregnancy body mass index (BMI). The only significant maternal factor was mean HbA1c levels, which were significantly higher in the GDM group compared with the controls at 5.04% (0.44) versus 4.83% (0.40) ( $p=0.018$ ). For the GDM group, the mean gestational age at diagnosis was 23.02 weeks (6.37). Of these, 30 women (60%) were managed with diet control alone, while 20 (40%) required pharmacologic treatment. Among those receiving medication, five were treated with oral agents only, and 15 received a combination of oral agents and insulin. Turning to ultrasound outcomes, ultrasound parameters were comparable between the GDM and non-GDM groups (Table 1).

**Table 1.** Comparison of demographic and clinical characteristics

	GDM (n=50)	Control (n=50)	p-value
Maternal age (years); mean [SD]	30.86 [5.39]	29.34 [6.39]	0.202
Thai; n (%)	26 (52)	34 (68)	0.102
Nulliparity; n (%)	20 (40)	21 (42)	0.83
Pre-pregnancy BMI (kg/m <sup>2</sup> ); mean [SD]	24.79 [4.87]	24.98 [4.47]	0.841
HbA1c (%); mean [SD]	5.04 [0.44]	4.83 [0.4]	0.018*
Gestational age at ultrasound scan (weeks); mean [SD]	30 [0.9]	29.98 [0.91]	0.913
BPD (cm); mean [SD]	7.5 [0.35]	7.49 [0.35]	0.873
HC (cm); mean [SD]	27.7 [0.95]	27.73 [1.04]	0.890
AC (cm); mean [SD]	25.85 [1.11]	25.62 [1.14]	0.301
FL (cm); mean [SD]	5.71 [0.31]	5.65 [0.25]	0.303
EFW (g); mean [SD]	1,503.6 [171.32]	1,467.76 [173.37]	0.301
DVP (cm); mean [SD]	4.54 [1.08]	4.44 [0.86]	0.619

AC=abdominal circumference; BMI=body mass index; BPD=biparietal diameter; DVP=deepest vertical pocket; EFW=estimated fetal weight; FL=femur length; GDM=gestational diabetes mellitus; HC=head circumference; SD=standard deviation  
p-values were calculated using the t-test or chi-square/Fisher's test, \* Statistical significance, p<0.05.

**Table 2.** Perinatal and neonatal outcomes in the two groups

	GDM (n=49)	Control (n=46)	p-value
Gestational age at birth (weeks); mean [SD]	38.33 [1.39]	38.7 [1.17]	0.166
Route of delivery; n (%)			0.194
Vaginal delivery	16 (32)	21 (42)	
Cesarean delivery	33 (66)	25 (50)	
Newborn weight (g); mean [SD]	3,115.65 [539.72]	3,144.67 [363.3]	0.758
Apgar score at 1 minute; mean [SD]	8.57 [0.9]	8.71 [0.8]	0.469
Apgar score at 5 minutes; mean [SD]	9.43 [0.73]	9.71 [0.77]	0.112
Apgar score at 5 minutes; n (%)	(n=37)	(n=38)	1
<7	0 (0)	1 (2)	
≥7	37 (74)	37 (74)	
Unknown	13 (26)	12 (24)	
Newborn complications; n (%)			
None	42 (84)	39 (78)	0.898
NIPPV	6 (12)	4 (8)	0.573
ETT	1 (2)	0 (0)	1
Sepsis	0 (0)	3 (6)	0.11
Unknown	1 (2)	4 (8)	0.147

ETT=endotracheal intubation; GDM=gestational diabetes mellitus; NIPPV=non-invasive positive pressure ventilation; SD=standard deviation  
p-values were calculated using the t-test or chi-square/Fisher's test, \* Statistical significance, p<0.05.

There were no significant differences in gestational age at scan, biparietal diameter, head circumference, abdominal circumference, femur length, estimated fetal weight, or deepest vertical pocket. These findings indicated that fetal biometry and amniotic fluid volume were similar across groups.

Perinatal and neonatal outcomes were similar between groups (Table 2). No significant differences were found in gestational age at delivery, delivery route, birthweight, or Apgar scores at 1 and 5 minutes. Neonatal complications, including the need for

non-invasive positive pressure ventilation (NIPPV), intubation, or sepsis, also did not differ significantly. Perinatal outcome data were available for 95 of 100 participants (95%), while five participants (5%) were lost to follow-up due to delivery in provincial hospitals and an inability to contact them. Follow-up spanned from enrollment at 29 to 32 weeks of gestation until delivery, with an average follow-up duration of 10 to 12 weeks.

Comparison of fetal brain structures between the GDM and control groups is presented in Table 3.

**Table 3.** Comparison of fetal brain structure ultrasound findings

	GDM (n=50); mean [SD]	Control (n=50); mean [SD]	Mean difference (95% CI)	p-value
CSP (mm)	6.03 [0.94]	6.19 [0.85]	-0.16 (-0.52 to 0.19)	0.366
PLV (mm)	5.45 [1.25]	4.69 [1.01]	0.76 (0.31 to 1.22)	0.001*
CM (mm)	6.36 [1.10]	6.21 [1.15]	0.15 (-0.29 to 0.6)	0.493
TCD (cm)	3.68 [0.26]	3.65 [0.24]	0.03 (-0.07 to 0.13)	0.560
Thalamus (cm)	2.02 [0.15]	2.03 [0.15]	-0.02 (-0.07 to 0.04)	0.597

CI=confidence interval; CM=cisterna magna; CSP=cavum septum pellucidum; GDM=gestational diabetes mellitus; PLV=posterior lateral ventricle; SD=standard deviation; TCD=transcerebellar diameter  
p-values were calculated using the independent t-test, \* Statistical significance,  $p < 0.05$ .

**Table 4.** Sensitivity and specificity of the PLV for predicting GDM

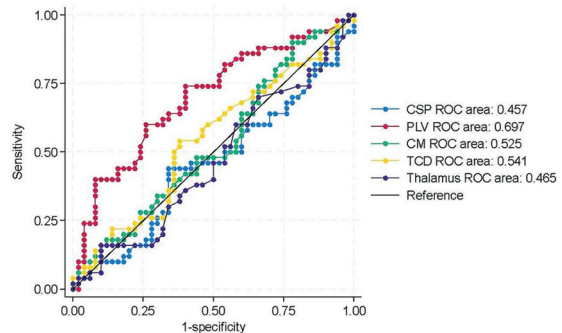
	Cutoff value (mm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	-LR	Accuracy (%)
PLV	4.6	74.0	60.0	64.9	69.8	1.85	0.43	67.0
	5.0	60.0	74.0	69.8	64.9	2.31	0.54	67.0

GDM=gestational diabetes mellitus; -LR=negative likelihood ratio; NPV=negative predictive value; PLV=posterior lateral ventricle; +LR=positive likelihood ratio; PPV=positive predictive value  
Cut-off values were determined using Youden's index.

The mean PLV was significantly larger in fetuses of mothers with GDM at 5.45 mm (1.25) than in controls at 4.69 mm (1.01). The mean difference was 0.76 mm (95% CI 0.31 to 1.22,  $p=0.001$ ). No significant differences were observed for other brain structures, including the mean CSP, mean CM, mean TCD, or mean thalamus (all  $p > 0.05$ ). These findings indicated that PLV enlargement was the only intracranial parameter associated with GDM in this cohort.

ROC curve analysis was performed to evaluate the ability of fetal brain structures to discriminate between GDM and non-GDM pregnancies (Figure 4). Of all the measurements, only the PLV demonstrated significant discriminative value, with an area under the curve (AUC) of 0.697 (95% CI 0.594 to 0.801,  $p=0.001$ ), indicating fair performance. In contrast, the CSP (AUC 0.457,  $p=0.454$ ), CM (AUC 0.525,  $p=0.664$ ), TCD (AUC 0.541,  $p=0.478$ ), and thalamus (AUC 0.465,  $p=0.542$ ) did not show significant discriminative ability. To further illustrate the diagnostic performance, Table 4 presents the optimal cutoff points for differentiating pregnancies with GDM from normal pregnancies. A PLV cutoff value of 4.6 mm yielded a sensitivity of 74%, specificity of 60%, positive predictive value (PPV) of 64.9%, negative predictive value (NPV) of 69.8%, and an accuracy of 67%. Increasing the cutoff to 5.0 mm improved specificity to 74% but reduced sensitivity to 60%, while predictive values and accuracy remained similar.

Table 5 presents the correlation analysis to assess the relationship between maternal mean HbA1c

**Figure 4.** ROC curves for the CSP, PLV, CM, TCD, and thalamus in identifying pregnancies with GDM. Only the PLV demonstrated significant discriminative ability (AUC 0.697, 95% CI 0.594 to 0.801,  $p=0.001$ ).

CM, cisterna magna; CSP, cavum septum pellucidum; GDM, gestational diabetes mellitus; PLV, posterior lateral ventricle; TCD, transcerebellar diameter

levels and various fetal brain measurements. Mean HbA1c showed positive correlations with the PLV ( $r=0.258$ ,  $p=0.009$ ) and CM ( $r=0.240$ ,  $p=0.016$ ), but no significant correlations were observed with CSP, TCD, or thalamic diameter.

## DISCUSSION

In the present prospective cohort study, the authors found that fetuses of mothers with GDM had significantly larger mean PLVs compared with those of non-diabetic mothers at 5.45 mm (1.25) versus 4.69 mm (1.01), ( $p=0.001$ ), while other intracranial structures did not differ between groups. The PLV size also showed a significant positive correlation

**Table 5.** Correlation analysis between maternal mean HbA1c levels and mean fetal brain measurements

Variables	HbA1c	
	r	p-value
CSP (mm)	0.177	0.079
PLV (mm)	0.258	0.009*
CM (mm)	0.240	0.016*
TCD (cm)	0.020	0.847
Thalamus (cm)	0.114	0.260

CM=cisterna magna; CSP=cavum septum pellucidum; PLV=posterior lateral ventricle; TCD=transcerebellar diameter  
Correlation coefficients (r) and p-values were calculated using Pearson's correlation coefficient, \* Statistical significance,  $p < 0.05$ .

with maternal HbA1c levels ( $r=0.258$ ,  $p=0.009$ ), indicating a link between maternal glycemic control and ventricular enlargement. Moreover, ROC analysis showed that the PLV had fair discriminative ability in differentiating GDM pregnancies from controls (AUC 0.697, 95% CI 0.594 to 0.801,  $p=0.001$ ), underscoring its potential as an early sonographic marker of altered fetal neurodevelopment in maternal diabetes.

Assessment of the LVs is a reliable indicator of fetal brain development, as it constitutes a fundamental measurement included in routine fetal anomaly scans<sup>(19)</sup>. The authors' observation of ventricular enlargement in fetuses of mothers with GDM aligns with prior studies reporting structural brain changes in diabetic pregnancies. Ruth Gründahl et al.<sup>(14)</sup> found that both the CSP and LVs were significantly larger in diabetic pregnancies. Similarly, Ekin & Sever<sup>(15)</sup> observed that the CSP, CM, and LVs were enlarged in diabetic pregnancies. Although individual studies have identified differences in other intracranial structures, enlargement of the LVs consistently emerges as a key and reproducible finding across investigations, reinforcing its potential as a sensitive sonographic marker of altered neurodevelopment in the context of maternal diabetes.

Additionally, Minowa et al.<sup>(20)</sup> found that slight LV dilatation on neonatal transfontanel ultrasound correlates with maternal diabetes, respiratory disturbance, and feeding hypoxemia, indicating in utero stress and underscoring the clinical relevance. Similarly, Tully et al.<sup>(21)</sup> linked neonatal hydrocephalus to maternal diabetes, especially pregestational diabetes, supporting the idea that fetal hyperglycemia increased cerebrospinal fluid (CSF) in the ventricles. Proposed mechanisms include obstruction at various sites or altered CSF dynamics. Maternal hyperglycemia may disrupt the

expression of genes critical for central nervous system development, causing obstructive malformations.

Overall, these studies support the concept that maternal diabetes is associated with altered fetal brain morphology. The specific brain structures involved vary across studies. Differences in study design, ethnicity, timing of fetal brain assessment, and whether GDM or pregestational, or pre-existing, diabetes populations are included may partly explain the heterogeneity of the findings. The present study adds to the literature by demonstrating a consistent association between maternal glycemic status as reflected by HbA1c, a marker of average blood sugar levels, and the size of the PLV in the fetal brain. The authors also demonstrate that the PLV exhibits fair discriminative ability in identifying GDM pregnancies.

The mechanisms by which maternal hyperglycemia alters fetal brain morphology remain unclear. Maternal diabetes causes chronic fetal hyperglycemia and hyperinsulinemia, leading to metabolic stress and impaired neuronal maturation<sup>(22)</sup>. Hyperglycemia-induced oxidative stress disrupts gene expression needed for brain development<sup>(22-24)</sup>. Experimental studies have shown that hyperglycemia interferes with neurogenesis and synaptogenesis, potentially impairing cognitive and motor outcomes later in life<sup>(13)</sup>.

Ventricular enlargement in fetuses of diabetic mothers may reflect altered CSF dynamics. This includes increased production, impaired absorption, or osmotic effects of maternal hyperglycemia. Prior studies have similarly reported enlargement of CSF-filled spaces in diabetic pregnancies<sup>(14-16)</sup>. Vascular and inflammatory pathways are also likely involved. Diabetes has been linked to oxidative stress, endothelial dysfunction, and microangiopathy. These changes may compromise the developing cerebral vasculature and disrupt normal brain maturation<sup>(22-24)</sup>.

The observed correlation between maternal HbA1c levels and PLV size in the present study further supports a dose-response relationship, whereby poorer glycemic control is associated with greater ventricular enlargement. This finding highlights the significance of optimal maternal glucose regulation for not only metabolic and obstetric outcomes but also early fetal neurodevelopment.

In the present study, perinatal and neonatal outcomes did not differ significantly between groups. This similarity may be explained by the fact that most women with GDM in the study were diet-controlled, and none had an HbA1c level greater than 6%. This

reflects good glycemic control, which could have contributed to the absence of differences in delivery outcomes or neonatal complications.

The present study's strengths include its prospective design, standardized ultrasound assessment within a narrow gestational window, and the use of maternal HbA1c to quantify glycemic status. These features strengthen the observed association between maternal diabetes and changes in fetal brain structure.

However, the present study has limitations. Its single-center design, modest sample size, and short recruitment period limit its generalizability and may introduce temporal bias. Sample size estimation based solely on CSP may have limited power for other brain structure comparisons. Residual confounding may persist because matching was performed only by gestational age. The two-step GDM diagnostic approach may have underestimated milder cases, and HbA1c was measured only once, potentially failing to fully reflect glycemic control throughout pregnancy. Ultrasound measurements were performed by a single unblinded operator, introducing potential measurement bias, while the narrow gestational age window of 29 to 32 weeks may limit assessment of brain growth variability.

As this was an exploratory study with a limited sample size, formal correction for multiple comparisons was not applied, which may increase the risk of type I error, but was intended to reduce the likelihood of missing true associations. Pearson's correlation analysis assumes linear relationships and may not fully reflect complex biological associations. Additionally, ROC-derived cutoffs from this modest sample size should be interpreted with caution. While strict exclusion criteria enhanced internal validity, they may have reduced real-world applicability. Finally, the lack of postnatal follow-up restricts conclusions on long-term neurodevelopmental outcomes.

## CONCLUSION

These findings suggest that maternal glycemic status during pregnancy may influence fetal brain development, particularly ventricular size, which can be assessed using ultrasound. Larger, longer studies are needed to clarify the clinical meaning of these changes and their impact on neurodevelopment.

## WHAT IS ALREADY KNOWN ABOUT THIS TOPIC?

Maternal diabetes is linked to structural and functional brain changes in offspring. These include

slight LV dilatation during the neonatal period and impaired neurodevelopmental outcomes. Fetal exposure to maternal diabetes also increases the long-term risk of obesity and metabolic disease.

## WHAT DOES THIS STUDY ADD?

This study shows that fetuses of mothers with GDM have larger PLVs, and this size is linked to maternal HbA1c levels. PLV size also helps identify GDM pregnancies, suggesting it is a sensitive sonographic marker of fetal neurodevelopmental changes related to maternal glycemic status.

## ACKNOWLEDGEMENT

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## AUTHORS' CONTRIBUTIONS

KC and PP were responsible for the conceptualization and design of the study. KC performed data collection, including clinical data acquisition and fetal imaging assessment, and curated the study database. KC and PP conducted the statistical analysis and interpreted the study results. KC drafted the original version of the manuscript. PP critically reviewed and revised the manuscript for important intellectual content and provided academic supervision throughout the study. Both authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

1. International Diabetes Federation. Gestational diabetes [Internet]. 2025 [cited 2025 Oct 1]. Available from: <https://idf.org/about-diabetes/types-of-diabetes/gestational-diabetes/>.
2. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. *Int J Mol Sci* 2018;19:3342. doi: 10.90/ijms19113342.
3. Fraser A, Lawlor DA. Long-term health outcomes in offspring born to women with diabetes in pregnancy. *Curr Diab Rep* 2014;14:489. doi: 10.1007/s11892-014-0489-x.
4. Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Spong CY, Hoffman BL, et al., editors. *Williams obstetrics*. 26th ed. New York: McGraw Hill Medical; 2022.

5. Lockwood CJ, Moore TR, Copel JA, Silver RM, Resnik R, Dugoff L, et al., editors. *Creasy & Resnik's maternal-fetal medicine: principles and practice*. 9th ed. Philadelphia, PA: Elsevier; 2023.
6. Fang P, An J, Tan X, Zeng LL, Shen H, Qiu S, et al. Changes in the cerebellar and cerebro-cerebellar circuit in type 2 diabetes. *Brain Res Bull* 2017;130:95-100.
7. Filip P, Canna A, Moheet A, Bednarik P, Grohn H, Li X, et al. Structural alterations in deep brain structures in type 1 diabetes. *Diabetes* 2020;69:2458-66.
8. Roy B, Ehlert L, Mullur R, Freeby MJ, Woo MA, Kumar R, et al. Regional brain gray matter changes in patients with type 2 diabetes mellitus. *Sci Rep* 2020;10:9925. doi: 10.1038/s41598-020-67022-5.
9. Biessels GJ, Reijmer YD. Brain changes underlying cognitive dysfunction in diabetes: what can we learn from MRI? *Diabetes* 2014;63:2244-52.
10. Hansen TM, Muthulingam JA, Brock B, Drewes AM, Juhl A, Vorum H, et al. Reduced gray matter brain volume and cortical thickness in adults with type 1 diabetes and neuropathy. *Neurosci Res* 2022;176:66-72.
11. Torres-Espinola FJ, Berglund SK, García-Valdés LM, Segura MT, Jerez A, Campos D, et al. Maternal obesity, overweight and gestational diabetes affect the offspring neurodevelopment at 6 and 18 months of age--a follow up from the PREOBE cohort. *PLoS One* 2015;10:e0133010.
12. Saros L, Lind A, Setänen S, Tertti K, Koivuniemi E, Ahtola A, et al. Maternal obesity, gestational diabetes mellitus, and diet in association with neurodevelopment of 2-year-old children. *Pediatr Res* 2023;94:280-9.
13. Rodolaki K, Pergialiotis V, Iakovidou N, Boutsikou T, Iliodromiti Z, Kanaka-Gantenbein C. The impact of maternal diabetes on the future health and neurodevelopment of the offspring: a review of the evidence. *Front Endocrinol (Lausanne)* 2023;14:1125628. doi: 10.3389/fendo.2023.1125628.
14. Ruth Gründahl F, Hammer K, Braun J, Oelmeier de Murcia K, Köster HA, Möllers M, et al. Fetal brain development in diabetic pregnancies and normal controls. *J Perinat Med* 2018;46:797-803.
15. Ekin A, Sever B. Changes in fetal intracranial anatomy during maternal pregestational and gestational diabetes. *J Obstet Gynaecol Res* 2023;49:587-96.
16. Guleroglu FY, Ocal A, Bakirci IT, Cetin A. Does diabetes mellitus affect the development of fetal brain structures and spaces including corpus callosum, subarachnoid space, insula, and parieto-occipital fissure? *J Clin Ultrasound* 2023;51:1483-91.
17. Rosner B. *Fundamentals of biostatistics*. 5th ed. Stamford: Duxbury Thomson Learning; 2000.
18. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. 15. Management of diabetes in pregnancy: Standards of care in diabetes—2023. *Diabetes Care* 2022;46 Suppl 1:S254-66.
19. Malinge G, Paladini D, Haratz KK, Monteagudo A, Pilu GL, Timor-Tritsch IE. ISUOG Practice guidelines (updated): sonographic examination of the fetal central nervous system. Part 1: performance of screening examination and indications for targeted neurosonography. *Ultrasound Obstet Gynecol* 2020;56:476-84.
20. Minowa H, Hirayama K, Arai I, Yasuhara H, Ebisu R, Ohgitani A. Clinical significance of slightly lateral ventricular enlargement in healthy infants. *J Matern Fetal Neonatal Med* 2017;30:1393-6.
21. Tully HM, Capote RT, Saltzman BS. Maternal and infant factors associated with infancy-onset hydrocephalus in Washington State. *Pediatr Neurol* 2015;52:320-5.
22. Dheen ST, Tay SS, Boran J, Ting LW, Kumar SD, Fu J, et al. Recent studies on neural tube defects in embryos of diabetic pregnancy: an overview. *Curr Med Chem* 2009;16:2345-54.
23. Wei D, Loeken MR. Increased DNA methyltransferase 3b (Dnmt3b)-mediated CpG island methylation stimulated by oxidative stress inhibits expression of a gene required for neural tube and neural crest development in diabetic pregnancy. *Diabetes* 2014;63:3512-22.
24. Fu J, Tay SS, Ling EA, Dheen ST. High glucose alters the expression of genes involved in proliferation and cell-fate specification of embryonic neural stem cells. *Diabetologia* 2006;49:1027-38.