ORIGINAL RESEARCH ARTICLE

Three-dimensional Power Doppler Ultrasonography Evaluation of Maternal Orbital Perfusion in Pregnancies with Gestational Diabetes Mellitus

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Abstract

Objective: Determine the level of maternal orbital perfusion in gestational diabetes mellitus (GDM) pregnant women using maternal orbital vascular sonobiopsy (MOVS) and three-dimensional (3D) power Doppler ultrasound methods.

Methods: The use of 3D power Doppler ultrasonography (3D-PDUS) for maternal orbital perfusion, together with virtual organ computer-aided analysis (VOCAL) histogram analysis, was carried out in 33 pregnancies between 25 and 40 weeks of gestation, including 18 cases of normal pregnancy (control) and 15 cases of gestational diabetes. The 3D power Doppler indices, such as the vascularization index (VI), flow index (FI), and vascularization FI (VFI), were calculated in both orbits of the individual group. The average value of each index for the two orbits was evaluated for further investigation. Both inter and intraobserver agreements of 3D-PDUS were examined.

Results: In the Bland–Altman test, the mean percentage difference and 95% limits of intra and interobserver agreements for VI, FI, and VFI were 0.0803% (7.3417, -7.181) and -0.6823% (10.8095, -12.1742), -0.4816% (6.0624, -7.0256) and 0% (9.0746, -8.8384), and 0.0058% (2.6937, -2.6821) and -0.2892% (3.8910, -4.4694), respectively. The correlation for all three 3D-PD indices, that is, VI, FI, and VFI, was higher than 0.75 (0.7832–0.9749). The VI, FI, and VFI levels between control and GDM pregnancies did not change significantly.

Conclusion: Our findings suggest that MOVS, which was assessed using 3D-PDUS and VOCAL histogram analysis, can offer fresh perspectives on observing maternal orbital perfusion in both healthy and dysfunctional pregnancies.

Keywords: Gestational diabetes mellitus, Maternal orbital perfusion, Maternal orbital vascular sonobiopsy, Normal pregnancy, Three-dimensional power Doppler ultrasound.

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Introduction

Hata et al.[1] research group reported the first discovery of maternal ophthalmic artery velocimetry during pregnancy. Furthermore, the maternal ophthalmic artery pulsatility index was considerably decreased in both hypertensive disorders of pregnancy (HDP)[2–5] and fetal growth restriction.[6] Moreover, the aforementioned index was also effective in type 1 DM.[7] MOV techniques are, therefore, a crucial criterion to comprehend the pathophysiology of many issues during pregnancy.

Gestational diabetes mellitus (GDM) affects only 5–8% of pregnancies worldwide.[8] GDM, which is typically caused by insulin resistance, is characterized by vascular dysfunction and the presence of subclinical inflammation.[9] Pregnancy-related GDM is probably a risk factor for developing type 2 diabetes as well as cardiovascular disease (CVD).[10] In general, type 2 diabetes is diagnosed in 60% of women with GDM within the next 5–16 years; however, this varies depending on other risk factors[11.] Endothelial dysfunction emerges immediately after

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Table 1: Clinical characteristics of subjects

Subject	*n*	*Maternal age* (*y.o*)	*Para*	*GA at examination* (*weeks*)	*Systolic BP* (*mm Hg*)	*Diastolic BP* (*mm Hg*)	*Mean BP* (*mm Hg*)	*Birth age* (*weeks*)	*Birth weight* (*gm*)	*Sex* (*male/female*)	*Apgar score*		*UApH*	*Delivery method*	*NICU admission*	*Neonatal abnormality*	*Maternal complication*
											1 minute	*5 minute*			(*VD/CS*)		
		Mean (*SD*)	*Median* (*range*)	*Mean* (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)	*Mean* (*SD*)		*Median* (*range*)	*Median* (*range*)	*Median* (*range*)	*Mean* (*SD*)	*n* (%)	*n* (%)	*n* (%)
Control	18	29.6 (5.9)	0 (0–2)	33.9 (3.8)	104.6 (11.6)	59.9 (6.6)	74.8 (7.6)	39.6 (1.0)	3191.0 (474.6)	(7/11)	9 (8–9)		9.5 (9–10)	7.32 (0.06)	(16/2)	2 (11.1)	1 (5.5)	0 (0)
GDM	15	33.0 (3.1)	0 (0–2)	34.4 (3.2)	114.8 (11.7)	69.6 (10.5)	84.6 (10.3)	39.5 (1.3)	3107.4 (282.2)	(6/9)	9 (3–9)		10 (9–10)	7.29 (0.07)	(10/5)	1 (6.6)	1 (6.6)	0 (0)
Significance		NS	NS	NS	$p < 0.05$	$p < 0.01$	$p < 0.01$	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS

BP, blood pressure; CS, cesarean section; GA, gestational age; GDM, gestational diabetes mellitus; NICU, neonatal intensive care unit; NS, not significant; SD, standard deviation; UApH, umbilical artery blood pH; VD, vaginal delivery; y.o., years old

Conflict of interest: Dr. Toshiyuki Hata is associated as the Scientific Editor of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of this Scientific Editor and his research group.

the onset of GDM and may be a risk factor for CVD.[12,13] GDM also has an impact on MOV during pregnancy.

The VOCAL application was used to quantify the placental perfusion using 3D-PDUS.[14,15] By using indices, that is, VI, FI including VFI of the 3D-PDUS technique,[16] data on utero and fetoplacental blood flows can be efficiently presented. We used the placental vascular sonobiopsy approach, which incorporates 3D-PDUS and VOCAL imaging histogram analysis for the qualitative and quantitative level evaluation of vascularization and blood flow in the placenta[17–20.] In our current study, we use 3D-PDU, which includes MOVS techniques, to assess maternal orbital perfusion in pregnancies associated with GDM. Additionally, 3D power Doppler indices using MOVS are used to assess inter and intraobserver agreements.

Materials and Methods

Patients

In the current cross-sectional investigation, 33 singleton pregnant women (control group, normal pregnancy, 18; and GDM, 15) were assessed between 25 and 40 weeks of gestation. It is noteworthy that GDM is defined by the International Association of Diabetes and Pregnancy Study Groups as glucose intolerance of any degree that begins or is first seen during pregnancy.[21] The only form of management for pregnant women with GDM was dietary therapy without the use of insulin. To determine the fetal age, the first-trimester crown-rump length measurement was used.[22] During the investigation, our study did not include preterm labor, antepartum hemorrhage, thyroid disease, maternal systemic disease, or HDP. Maternal age, para, gestational age at examination, systolic, diastolic, and mean blood pressure, gestational age at birth, birth weight, neonatal sex, delivery method and appearance, pulse, grimace, activity, and respiration (Apgar) score at 1/5 minute, umbilical arterial pH (UApH), neonatal intensive care unit (NICU) admission, neonatal abnormality, as well as maternal complications were all displayed in Table 1. All of the chosen women received a thorough description of the study before giving their informed consent, which was approved by the Miyake Clinic's ethics committee in Okayama, Japan.

Ultrasound Examination

All 3D-PD scans were performed in the current study by one trained examiner (RT) using a curved array transabdominal transducer, that is, GE eM6C G2, 2–7 MHz and Voluson E10 BT21 of GE Healthcare from Zipf, Austria. A 3D-PD scan

is performed on a typical MOV tree volume for each unique orbit. In each test, a pulse repetition frequency of 0.9 kHz was used, along with a wall motion filter set to "low 1" for maximum sensitivity. Frequency, low; dynamic, balance, 225; smooth, 4/4; ensemble, 8; power Doppler map, 2; artifact suppression, on; power Doppler line filter, 3; and quality, high were the fixed default instrument settings for all testing. The eye socket, which houses the eyeball and orbital cavity, was above each power Doppler window. Over the area with the highest villous vascular density, the 3D volume box was placed at a fixed 40° angle.

The mother was kept as motionless as possible throughout the volume acquisition process, which lasted five seconds for one measurement. A total of 1–3 3D-PD investigations were performed for each orbit, taking <1 minute for both orbits. The mechanical index (MI) ranged from 0.8 to 1.1, and the thermal index (TI) varied from 0.3 to 0.4.

The hard drive's volume data were recovered, and a multiplanar system was used to process them. By using the work pattern depicted in Figure 1, the boundaries of a virtual reference axis were located between the medial and lateral bones and behind the eyeball. The volume of a sphere was then determined and calculated by automatically revolving around this axis. Using the VOCAL application, as illustrated in Figure 2, the resulting sphere automatically aids in calculating color values such as VI, FI, and VFI. To evaluate blood flow and vessels, the aforementioned technology can acquire 3D-PD indices.[14,23]

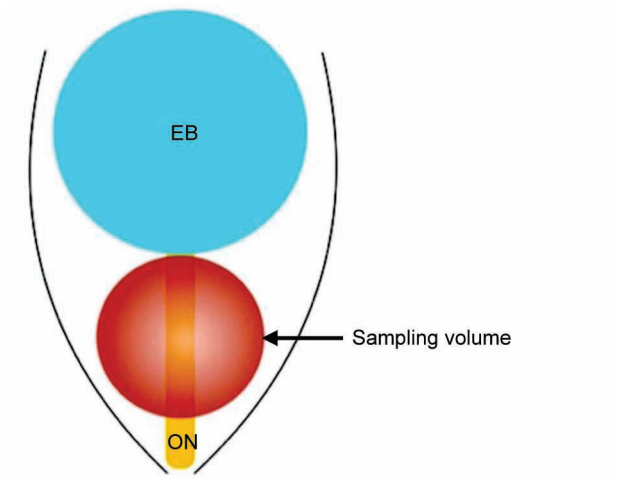

Fig. 1: Schematic image of MOVS. The light brown circle indicates the sampling volume. EB, eyeball; ON, optic nerve

Each subject's average values from both orbits were used to calculate the indexes.

Statistical Analysis

All analyses are performed with the aid of Wolfram Research Mathematica 13.0.0.0 software from Champaign, Illinois, United States of America. Unpaired *t*-tests were used to analyze any differences between the control and GDM groups in terms of maternal age, gestational age at examination, systolic, diastolic, mean blood pressures, birth age/weight, umbilical artery blood pH, as well as for VI, FI, and VFI. Mann–Whitney *U* tests compared the values of the para and Apgar scores between groups. Additional Chi-squared tests were run to compare the sex ratio, delivery technique, admission rates to NICU, and admission rates for neonatal abnormalities, including the occurrence of maternal complications. The intraclass correlation, or the intraclass correlation coefficient, was used to assess reliability.[15]

The intraclass correlation, or the intraclass correlation coefficient, was defined as the correlation between any two measurements derived from the same data. All values were discovered in the 0–1 range, with 1 denoting the best reliability. The inter and intraobserver variabilities were calculated over 38 samples (18 orbits in nine control and 20 orbits in GDM-related pregnancies) using Bland and Altman's methods.[24] The intraobserver variance was provided by RT, while the interobserver variation was provided by RT and TH. The average individual agreement gap is determined to be 2.0 standard deviations (SD), which aids in determining the 95% confidence intervals between them. The difference between the mean difference and zero can be examined

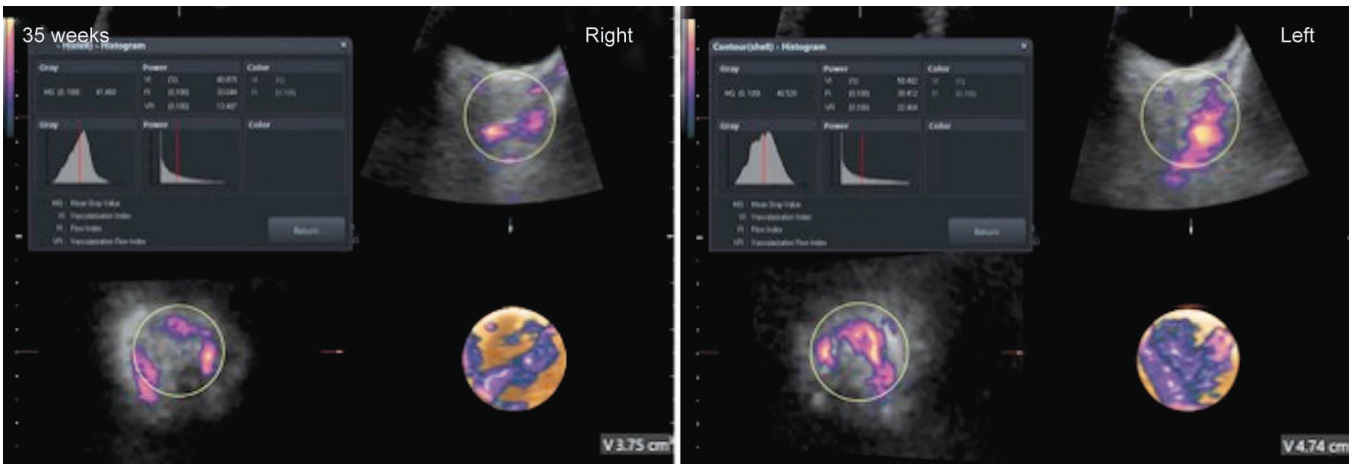

Fig. 2: 3D-PDUS measurements of left and right maternal orbital blood flows at 35 weeks of gestation. The VOCAL histogram analysis automatically calculates color values (VI, FI, and VFI) from the acquired sphere in each orbit. Left, left orbit; Right, right orbit

using the two-sample *t*-test. Finally, the *p*-value was considered to be somewhat significant when it was <0.05.

Results

In comparison to the control group, the GDM group exhibits higher systolic, diastolic, and mean blood pressures, which is supported by $p < 0.05$. But as can be seen in Table 1, neither group exhibit significant differences in the following variables—mother age, para, gestational age at delivery, birth age or weight, sex ratio, Apgar scores between 1 and 5 minutes, delivery mode, UApH, NICU hospitalization, neonatal abnormalities, and maternal complication.

Three neonates from each group were admitted to the NICU due to temporary tachypnea of the newborn. Small ventricular septal defects and polydactyly were two infant abnormalities found in the control and GDM groups, respectively. After inspection, no mother had any complaints about visual disturbances.

As shown in Tables 2 and 3, it was discovered that observer agreements, as well as intraclass correlation, or the intraclass correlation coefficients, are present. Thus, just one examiner (RT) evaluated the statistical examination data.

According to Table 4, there were no appreciable differences in the VI, FI, or VFI values for MOVS between control and GDM pregnancies (Figs 3 to 5).

Discussion

Maternal orbital perfusion may be measured using the MOVS technique, which also applies VOCAL histogram analysis and 3D-PDUS. The test's repeatability and excellent inter and intraobserver agreement are both demonstrated by MOVS. The aforementioned techniques were also straightforward, quick to

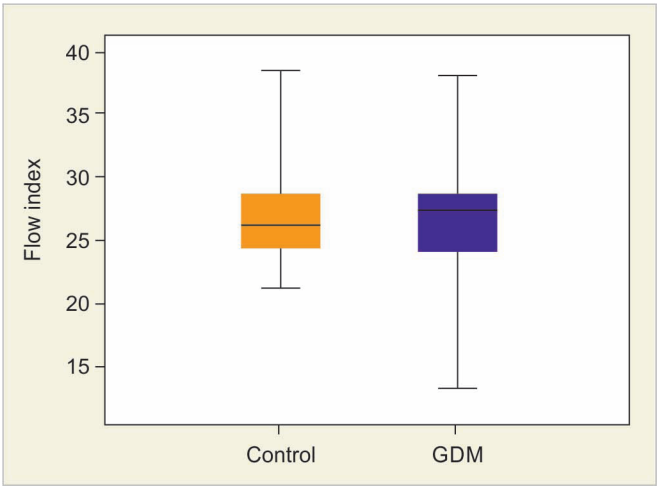

Fig. 4: Box plot of maternal orbital FI in normal (control) and GDM pregnancies. The black horizontal bar indicates the mean. Yellow and blue boxes are SD

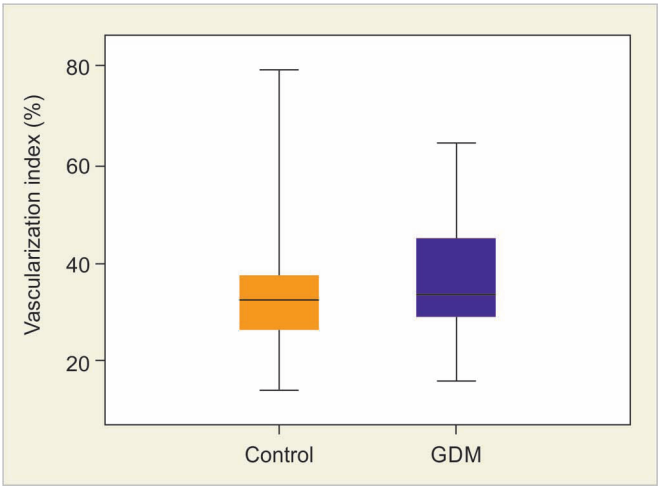

Fig. 3: Box plot of maternal orbital VI in normal (control) and GDM pregnancies. The black horizontal bar indicates the mean. Yellow and blue boxes are SD

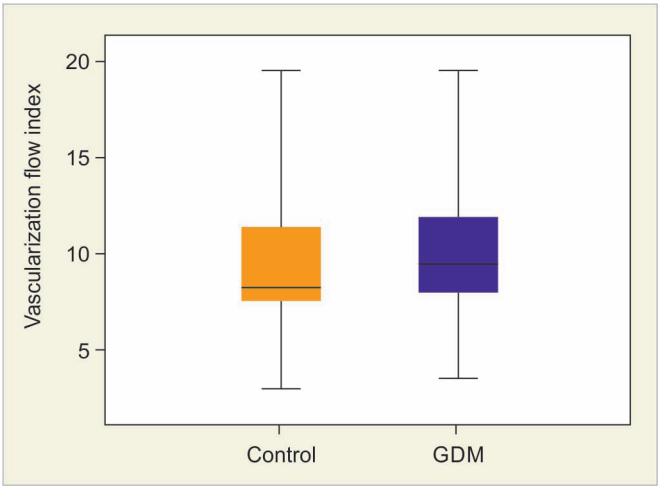

Fig. 5: Box plot of maternal orbital VFI in normal (control) and GDM pregnancies. The black horizontal bar indicates the mean. Yellow and blue boxes are SD

Table 2: Intraclass correlation coefficient and intraobserver agreement for maternal orbital vascularity indices

Parameters	*Mean difference*	*95% CI*	*Limits of agreement*	*p-value*	*ICC*	*p-value*
VI	**0.0803**	**−1.0976–1.2583**	**−7.1810–7.3417**	**0.894**	**0.9749**	**<0.0001**
FI	**−0.4816**	**−1.5431–0.5799**	**−7.0256–6.0624**	**0.380**	**0.8882**	**<0.0001**
VFI	**0.0058**	**−0.4302–0.4418**	**−2.6821–2.6937**	**0.979**	**0.9704**	**<0.0001**

95% CI, 95% confidence interval; FI, flow index; ICC, interclass correlation coefficient; VFI, vascularization flow index; VI, vascularization index

Table 3: Interclass correlation coefficient and interobserver agreement for maternal orbital vascularity indices

Parameter	*Mean difference*	*95% CI*	*Limits of agreement*	*p-value*	*ICC*	*p-value*
VI	**−0.6823**	**−2.5465–1.1818**	**−12.1742–10.8095**	**0.478**	**0.9364**	**<0.0001**
FI	**0**	**−1.3348–1.5710**	**−8.8384–9.0746**	**0.874**	**0.7832**	**<0.0001**
VFI	**−0.2892**	**−0.9673–0.3889**	**−4.4694–3.8910**	**0.409**	**0.9214**	**<0.0001**

95% CI, 95% confidence interval; FI, flow index; ICC, interclass correlation coefficient; VFI, vascularization flow index; VI, vascularization index

Table 4: Comparison of maternal orbital Doppler indices between control and gestational diabetes mellitus pregnancies

		VI (%)	*FI*	*VFI*
Subject	*n*	*Mean (SD)*	*Mean (SD)*	*Mean (SD)*
Control	**18**	**33.8 (14.5)**	**27.2 (4.2)**	**9.3 (4.0)**
GDM	**15**	**36.4 (12.6)**	**27.0 (5.8)**	**10.3 (4.2)**
Significance		NS	NS	NS

FI, flow index; GDM, gestational diabetes mellitus; NS, not significant; VFI, vascularization flow index; VI, vascularization index

perform, and easy to examine. Due to its simplicity, accuracy, and objectivity, conventional ocular artery velocimetry was used to assess MOV.[25] To understand the ocular artery, particularly ophthalmic artery blood flow velocity waveforms, however, further research is needed in HDP.[26]

In pregnancies with different difficulties, MOVS may be a more helpful diagnostic method to evaluate the vascularity and blood flow in the mother's orbits. To effectively use MOVS to assess the blood flow and maternal ocular vascularity in various pregnancy difficulties under clinical practice and long-term endurance, more research was needed.

Pregnant women with GDM had widespread endothelial dysfunction, which led to higher vascular resistance and less effective vasodilation[27,28]. Therefore, in GDM pregnancies, reduced maternal orbital perfusion may be taken into account. In this study, it was revealed that there were no appreciable differences in values for VI, FI, or VFI between control and GDM pregnancies.

At this time, the cause of these results is unknown. This aberration may be brought on by a variation in the level of extreme GDM. All investigations into GDM-related pregnancies were successfully managed by nutrition therapy alone, without the use of supplementary insulin therapy.

Consequently, our GDM pregnancies could be of moderate variety. The extra factor could be the smaller sample size. More research with a larger number of participants is required to characterize and document the small decline in maternal orbital perfusion in pregnancies associated with GDM.

Due to the delicate tissues of the orbital cavity, bioeffects, and safety concerns are essential factors in orbital Doppler tests.[29] Here, the 3D-PD TI values were 0.3 or 0.4 (<1), and the MI values ranged from 0.8 to 1.1 (around 1). Examining was done using the examination with exposure as low as reasonably achievable (ALARA) approach, and the 3D-PD procedure was brief (<1 minute in our study).[30] For Doppler studies, including orbital examinations, it is crucial to keep exposure times as brief as feasible and use the lowest sonic output permitted for adequate diagnostic acuity. The bioeffects and safety of an orbital Doppler examination will be improved by further technical developments in Doppler ultrasound.

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