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Pregnancy and post-partum muscle and cerebral oxygenation during intermittent exercise in gestational diabetes: A pilot study

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ABSTRACT

Objective: This pilot, prospective, observational, cohort study aimed to examine, for the first time, the in vivo alterations in the oxygenation of the forearm skeletal muscles and the prefrontal lobes during intermittent exercise in women diagnosed with gestational diabetes mellitus (GDM), during and after pregnancy.
Study Design: Nine pregnant women, diagnosed with GDM, performed a 3-min intermittent handgrip exercise protocol (at 35% of Maximal Voluntary Contraction) during pregnancy (mean 27th gestational week) and following labor (mean 71 weeks). During the protocol, muscle and cerebral oxygenation were assessed with near-infrared spectroscopy. Resting vascular parameters [carotid intima-media thickness (cIMT) and hemodynamic parameters (using rheocardiography)], and hematological/biochemical parameters during pregnancy and after delivery have been compared.
Results: Although changes were observed in certain hematological parameters ($p < 0.05$), cIMT and hemodynamic parameters were not altered post-partum. In addition, both muscle and cerebral oxygenation parameters during handgrip were not significantly altered post-partum.
Conclusions: Despite significant changes in specific hematological parameters in women with GDM, impairments in muscle and cerebral oxygenation during exercise remained at one year after labor. These results indicate that alterations in vascular parameters and muscle/cerebral oxygenation associated with GDM do not entirely reverse post-partum. Future studies are needed to examine which interventions will lead to improvements in microvascular parameters and prevent type 2 diabetes.

Introduction

Gestational Diabetes Mellitus (GDM) is a condition first diagnosed in the second or third trimester of pregnancy, without any evidence of pre-existing type 1 (T1DM) or type 2 diabetes (T2DM) [1]. A variety of factors can contribute to the development of GDM, such as obesity, weight gain throughout pregnancy, family history of diabetes mellitus (DM) and previous history of GDM, older maternal age, fetal macrosomia, unexplained still birth and the ethnicity of the woman in pregnancy [2]. The manifestation of GDM is reported in approximately 7% of all pregnancies, with a prevalence ranging from 1 to 14%, based on study population and implemented diagnostic tests [3].

Pregnancy in GDM patients is usually accompanied by progressive insulin resistance compared with the insulin resistance observed in patients with T2DM [4]. However, the resistance mentioned above is normalized immediately after delivery, indicating that the primary pathophysiological mechanism is placental hormones [4]. Although it is a pregnancy complication that usually resolves after birth, GDM has been associated with many short- and long-term health consequences for both the newborn and the mother [5,6].

Women with previous pregnancy-induced hyperglycemia demonstrated higher concentrations of endothelial dysfunction markers compared with those with unaffected pregnancies [7]. These values have been associated with an increased probability of future cardiovascular risk, as it might be assumed that GDM and

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cardiovascular disease (CVD) share mutual disease mechanisms [7]. It has been demonstrated that GDM is associated with increased carotid intima-media thickness (cIMT) [8]. This association is stronger in obese women with GDM and is already present at the time of pregnancy, suggesting the efficacy of weight control in women with GDM to prevent CVD [8].

Impaired tissue oxygen (O_2) delivery, as a cause of diabetic microangiopathy, has been regarded as one of the initiating events during the progression of DM [9]. Near-infrared spectroscopy (NIRS) is widely used for the assessment of blood flow, oxygen availability and metabolic responses to exercise in multiple tissues, such as the muscle, the brain or the connective tissue [10]. Using NIRS, a recent study showed that women with GDM presented blunted microvascular reactivity and alterations in skeletal muscle oxygenation compared with women with uncomplicated pregnancies that were associated with indices of cardiovascular risk [11]. In addition, changes in muscle oxygenation were manifested during exercise, and possibly contributed to the lower exercise tolerance in GDM [11]. Furthermore, another study has shown that cerebral oxygenation during exercise was also reported to be significantly impaired in women with GDM compared with uncomplicated pregnancies [12].

To our knowledge, no study so far has assessed both muscle and cerebral oxygenation during exercise in women with GDM and examined whether it improves following labor. With this in mind, the purpose of this study was to assess oxygenation of the forearm skeletal muscles and the prefrontal lobes during intermittent handgrip exercise, in women diagnosed with GDM, during pregnancy and post-partum.

Methods

Study characteristics

Pilot, prospective, observational, cohort study.

Participants

The study included nine (n = 9) pregnant women, referred to the Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, during 2016–2017, and diagnosed with GDM, according to the criteria of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG). GDM was diagnosed by a 75 g oral glucose tolerance test (OGTT), when at least one of the following values had been exceeded: fasting glucose $\geq$92 mg/dl (5.1 mmol/l); 1-hour plasma glucose $\geq$180 mg/dl (10.0 mmol/l); or 2-hour plasma glucose $\geq$153 mg/dl (8.5 mmol/l) [13]. Patients have been assessed twice, during pregnancy (mean 27th gestational week) and following labor (mean 71st week).

An established diagnosis of T2DM following labor was based on the American Diabetes Association (ADA) criteria: fasting plasma glucose $\geq$126 mg/dl (7.0 mmol/l), 2-hour plasma glucose $\geq$ 200 mg/dl (11.1 mmol/l) or $HbA_{1c} \geq$ 6.5% (48 mmol/mol) [1].

This study has been approved by the institutional review board committee and it was conducted in accordance to the Helsinki Declaration (1975, 1983 revision). Before the enrollment in the study, a written informed consent form has been signed by each participant.

Patient inclusion criteria were 1) age $\geq$18 years, 2) otherwise healthy (absence of any CVD), and 3) having signed informed consent. Women meeting the following criteria were excluded from the study: 1) pre-existing DM, 2) infections or any type of inflammation, 3) co-morbidities (neoplasms, uncontrolled systemic diseases); 4) use of prohibited substances. Patients were instructed to avoid alcohol or caffeine intake and intense physical activity for at least 18 h.

Pre-exercise assessment

Both during the first assessment and re-assessment, participants attended the Hypertension Unit of the Third Department of Internal Medicine, Papageorgiou Hospital, of Aristotle University. For each woman with GDM enrolled in the study, a full personal, obstetric, family and social history was obtained. During clinical examination, somatometric data including height, weight and body mass index (BMI) at the day of admission to the study and following labor, pregnancy and post-partum systolic and diastolic blood pressure at rest and heart rate were recorded. An OGTT with 75 g of glucose has been performed with a glucose measurement at 0 and 120 min both during pregnancy and following labor. A thorough hematologic and biochemical screening has been performed. Hematocrit (Ht), hemoglobin (Hb), platelets (PLT), glucose, insulin resistance based on homeostasis model assessment of insulin resistance (HOMA-IR), thyroid stimulating hormone (TSH), total, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) were recorded during and after pregnancy. Out of nine participants, one did not complete the post-partum hematologic/biochemical screening.

Macro-circulation assessment

The estimation of cIMT, a non-invasive biomarker for arteriosclerosis and vascular thickening, was carried out by a B-mode carotid ultrasound with participants in the supine position. The ultrasound device employs digital imaging to estimate the thickness of the inner two layers of the common carotid artery and identify if plaques are present. Total cIMT was assessed as a mean value of the right and left common artery, both during pregnancy and post-partum.

Impedance rheocardiography (REO/ICG) was used to non-invasively assess resting hemodynamic parameters, as previously described [14]. A large variety of parameters have been estimated focusing on systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), heart rate (HR), stroke index (SI), cardiac index (CI) and systemic vascular resistance index (SVRI).

Exercise protocol

Skeletal muscle and cerebral oxygenation was assessed by measuring the micromolar (μM) relative changes in oxygenated (HbO_2), de-oxygenated (HHb), and total hemoglobin (tHb) using NIRS (Oxymon, Artinis Medical Systems) and handgrip force was assessed using a digital dynamometer (MP150, Biopac, Goleta, CA, USA). Initially, the participant's Maximal Voluntary Contraction (MVC) was measured with three trials (a 90 s rest between attempts) in the seated position, and the elbow flexed at 90°. Subsequently, the participant performed the 3-min intermittent exercise protocol (4 s exercise at 35% MVC with a 3 s rest), during which she had visual feedback to maintain force output to the predetermined percentage of her MVC. During this protocol, the NIRS device was placed at the participant's fore arm to non-invasively monitor skeletal muscle oxygenation, and another NIRS sensor was placed over the prefrontal cortex (contralaterally of the exercising arm), 2 cm beside the midline and about 3 cm above the supra orbital ridge to assess cerebral oxygenation. The rate of perceived exertion (RPE) was assessed in a 6–20 scale at the termination of exercise. Out of nine participants, one refused to be reassessed with NIRS during the post-partum assessment.

Statistical analysis

Statistical analysis was performed with the use of R Studio 1.0.153 Software. All variables acquired from NIRS have been averaged over the testing periods (Oxysoft, Artinis Medical Systems, Elst, the Netherlands). Categorical variables have been expressed as percentages. The level of statistical significance was set at 0.05. Normality was assessed with the use of the Shapiro-Wilk test, since the number of observations was lower than 50, to decide upon the selection of a parametric or non-parametric analysis. Continuous variables have been expressed using median values and interquartile range (IQR), for non-normally distributed data. The Wilcoxon Signed Rank non-parametric test was applied to identify any changes in the data obtained during pregnancy and those obtained after delivery in women with GDM. Finally, the Pearson correlation coefficient was applied to assess possible linear correlations between specific variables.

Results

Pregnancy baseline characteristics/patient history

Participants' median age was 37 years (IQR 4.00), median parity was 1.00 (2.00), and median gravidity was 2.00 (2.00).

Pregnancy outcome

Following delivery, none of the participants reported any complications during labor. Median birth gestational week was 38.0 (0.5), and median neonatal weight was 3270 (360) g. One-third of the participants reassessed post-partum were receiving medication for hypothyroidism or anemia, while 44% were breastfeeding.

Pregnancy versus post-partum biochemical, metabolic, and macrovascular parameters

The participants hematological/biochemical results are presented in Table 1. Significant changes following labor compared to those obtained during pregnancy were observed in Ht, Hb and PLT. cIMT values and hemodynamic data from REO/ICG are presented in Table 2.

Table 1
Baseline characteristics and test results in women with GDM (pregnancy and post-partum).

Variables	Pregnancy	Post-GDM	*p*-value
Baseline characteristics (n = 9)			
Week of assessment	27.4 (2.9)	74.0 (37.0)	N/A
Weight (kg)	78.0 (24.0)	79.8 (36.4)	0.29
BMI (kg/m^2)	31.0 (8.4)	27.6 (12.1)	0.25
Resting systolic BP (mm Hg)	114 (18)	111 (12)	0.20
Resting diastolic BP (mm Hg)	70.0 (8.0)	74.0 (8.5)	0.34
Heart rate (beats/min)	88.5 (6.0)	73.5 (6.25)	0.25
Test results (n = 8)			
OGTT at 0 min (mg/dl)	95.0 (4.0)	89.0 (13.0)	0.50
OGTT at 120 min (mg/dl)	146 (67)	102 (22)	0.50
Glucose (mg/dl)	78.0 (9.5)	95.0 (6.0)	0.13
Ht (%)	35.3 (4.1)	39.2 (4.7)	**0.04**
Hb (g/dl)	11.0 (1.6)	13.0 (1.6)	**0.04**
SGOT (U/l)	15.5 (5.3)	17.0 (4.3)	0.58
SGPT (U/l)	10.5 (3.8)	18.5 (15.8)	0.63
PLT (10^3/ml)	200 (52)	269 (82)	**0.03**
TSH (mIU/l)	1.45 (0.64)	2.07 (0.57)	0.75
TC (mg/dl)	253 (69)	189 (78)	0.31
HDL-c (mg/dl)	67.0 (14.5)	65.0 (22.0)	0.44
LDL-c (mg/dl)	149 (51)	136 (69)	0.56
HOMA-IR	2.2 (3.8)	2.5 (1.2)	0.99

Variables are expressed as median (interquartile range).
BMI: body mass index; BP: blood pressure; GDM: gestational diabetes mellitus; HDL-c: high-density lipoprotein cholesterol; Ht: hematocrit; Hb: hemoglobin; LDL-c: low-density lipoprotein cholesterol; N/A: not-applicable; OGTT: oral glucose tolerance test; PLT: platelet count; SGOT: serum glutamic oxaloacetic transaminase; SGPT: serum glutamic pyruvic transaminase; TC: total cholesterol; TSH: thyroid-stimulating hormone; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance.

Table 2
Macrovascular assessment in women with GDM (pregnancy and post-partum).

Variables	Pregnancy	Post-GDM	*p*-value
Carotid IMTm (mm)	0.52 (0.14)	0.51 (0.05)	0.57
Rheocardiography			
SBP (mm Hg)	101.0 (14.0)	111.0 (1.5)	0.59
DBP (mm Hg)	64.0 (10.0)	70.0 (3.0)	0.75
MBP (mm Hg)	76.0 (9.0)	83.0 (2.0)	0.75
HR (1/min)	86.0 (6.0)	64.0 (2.5)	0.25
SI (ml/m^2)	48.0 (9.0)	63.0 (7.5)	0.25
CI (l/min/m^2)	3.8 (0.3)	3.9 (0.4)	0.17
SVRI (dyn.s. cm^{-5} m^2)	1417 (305)	1418 (238)	0.25

Variables are expressed as median (interquartile range).
GDM: gestational diabetes mellitus; IMTm: intima-media thickness mean; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; HR: heart rate; SI: stroke index; CI: cardiac Index; SVRI: systemic vascular resistance index.

Pregnancy versus post-partum muscle/cerebral oxygenation during exercise

In pregnancy, muscle TSI significantly decreased ($p < 0.05$) during exercise compared to resting/baseline levels (-2.44, IQR: 2.71) Similarly, post-GDM muscle TSI significantly decreased ($p < 0.05$) during exercise compared to resting/baseline levels (-2.84, IQR:4.69). However, no significant differences were observed in the average TSI decline during exercise between the pre- and post-partum measurements ($p = 0.64$) (Fig. 1). Only the TSI area under the curve was significantly greater in pregnancy vs. post-partum (11,352, IQR: 1157 vs 12,348, IQR: 1433; $p = 0.01$). Furthermore, no significant differences were observed in the average HbO_2 decline, HHb increase, and tHb during handgrip, between the pre- and post-partum measurements. Handgrip strength pregnancy values were relatively similar ($p = 0.08$) with those obtained post-partum (average percentage of force maintained during the 3-min handgrip: 22%, IQR: 1% vs. 26%, IQR:4%, respectively). Median RPE during pregnancy was 13.25 (2.00) and was reduced to 11.75 (1.88) post-partum, though not in a significant manner (p=0.14) (Table 3).

Correlation between glucose and muscle/cerebral oxygenation

Finally, a possible linear correlation was assessed between OGTT glucose at time 0 min and NIRS exercise variables both during pregnancy and post-partum. Since no significant correlation was found between the variables, no further regression analysis was conducted (Table 4).

Discussion

Main findings

This study provided novel evidence regarding the alterations in both muscle and cerebral oxygenation during intermittent exercise, as assessed by NIRS, in women diagnosed with GDM, during pregnancy and post-partum. Regardless of the significant changes in specific hematological parameters, the impaired muscle and cerebral oxygenation during exercise persisted even one year following labor. These findings indicate that alterations in vascular parameters and tissue oxygenation attributed to GDM are not entirely reversed post-partum.

Comparison to literature

The NIRS method is widely used in research, as it can assess dynamic alterations in the levels of tissue HbO_2 and HHb, total blood volume (tBV) and can reflect the oxidation state of the

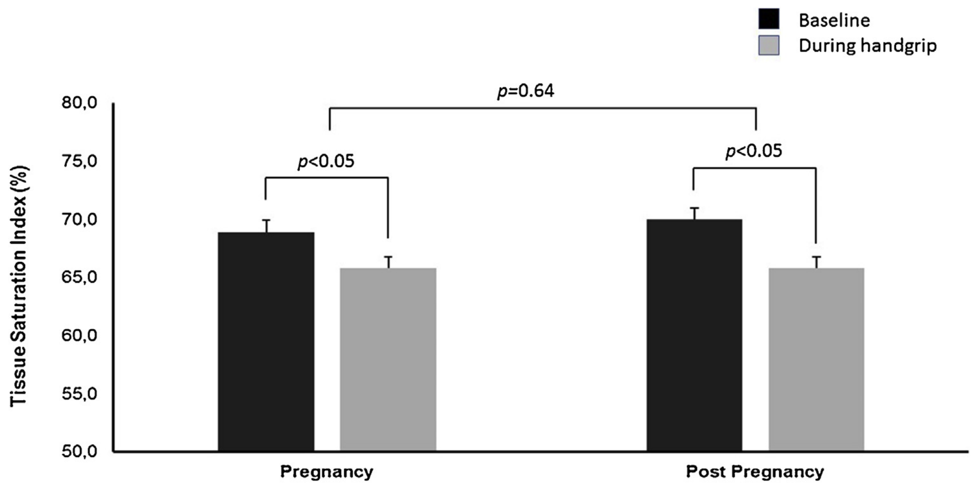

Fig. 1. Muscle oxygen saturation index (TSI, %) at baseline and during handgrip exercise (average 3-min response), as assessed by NIRS during pregnancy and following labor (Post-GDM) (n = 8). TSI: tissue saturation index.

copper moiety (CuA) of mitochondrial cytochrome C oxidase (cytochrome *A*, A3) in the skeletal muscle [15]. The NIRS technology has been applied for the assessment of cerebral tissue hemoglobin levels during the peripartum period in both complicated and uncomplicated pregnancies [16]. NIRS has also been used for the evaluation of placental oxygenation and neonatal brain and peripheral tissue oxygenation during birth [17,18].

Table 3
Muscle/cerebral oxygenation parameters assessed by NIRS.

NIRS variable	Pregnancy	Post-GDM	*p*-value
Skeletal muscle oxygenation			
HbO_2 average response	−0.57 (1.37)	−0.89 (3.64)	0.38
HbO_2 AUC	192 (147)	330 (279)	0.25
HHb average response	1.16 (1.29)	1.38 (3.14)	0.95
HHb AUC	195 (189)	250 (578)	0.84
tHb average response	2.41 (2.29)	1.31 (2.67)	0.55
tHb AUC	444 (171)	382 (384)	0.95
Cerebral oxygenation			
HbO_2 average response	1.29 (1.53)	1.39 (1.05)	0.99
HbO_2 AUC	236 (268)	254 (193)	0.84
HHb average response	−0.64 (0.49)	−0.29 (0.33)	0.25
HHb AUC	−93.4 (77.0)	−52.0 (57.0)	0.38
tHb average response	1.05 (1.81)	1.04 (1.30)	0.99
tHb AUC	171 (310)	190 (235)	0.99

Variables are expressed as median (interquartile range) and expressed in μmol/l. NIRS: near-infrared spectroscopy; GDM: gestational diabetes mellitus; TSI: tissue saturation index; AUC: area under curve; HHb: deoxy-hemoglobin; HbO_2: oxy-hemoglobin; tHb: total hemoglobin (n = 8).

Maximal hand grip strength has been regarded as a strong indicator of muscle strength as well as muscle weakness and atrophy and a promising tool for assessing the overall quality of life [19].

As far as muscle oxygenation in women with GDM is concerned, a study implementing NIRS indicated that these women presented impaired muscle oxygenation and microvascular function during exercise as a cause of the increased exercise intolerance in GDM, as compared to women with uncomplicated pregnancies [11].

In this study, although there was an improvement in four out of eight participants in muscle TSI during exercise, the average improvement was not significant. In addition, although there was a trend for an increase in the force maintained during handgrip, this improvement was also not statistically significant.

As for cerebral oxygenation, it has been demonstrated that exercise underlines the imminent disorders of neuronal oxygenation and hemodynamics in the prefrontal cortex of patients with T1DM with poor disease control [20]. A recent study comparing uncomplicated with GDM-complicated pregnancies demonstrated that impaired cerebral oxygenation was present in complicated pregnancies and that cerebral oxygenation during exercise was correlated with macrovascular function and cardiovascular risk factors [12]. In this study, cerebral HbO_2, HHb and tHb values were improved post-partum, however, not in a significant manner.

During exercise, the impaired skeletal muscle oxygenation reported in patients with DM [21] was also observed in women

Table 4
Linear correlations between glucose and muscle/brain oxygenation.

	Correlation among variables (Pearson)		*p*-value
Muscle oxygenation during exercise	OGTT 0 – pregnancy	Pregnancy TSI average response	0.26
	OGTT 0 – pregnancy	Pregnancy percentage of MVC	0.27
	OGTT 0 – post-partum	TSI average response – post-partum	0.67
	OGTT 0 – post-partum	Percentage of MVC – post-partum	0.33
Brain oxygenation during exercise	OGTT 0 – pregnancy	Pregnancy HbO_2 average response	0.82
	OGTT 0 – pregnancy	Pregnancy HHb average response	0.14
	OGTT 0 – pregnancy	Pregnancy tHb average response	0.88
	OGTT 0 – post-partum	HbO_2 average response – post-partum	0.92
	OGTT 0 – post-partum	HHb average response – post-partum	0.31
	OGTT 0 – post-partum	tHb average response – post-partum	0.69

MVC: Maximal Voluntary Contraction; HbO_2: oxy-hemoglobin; HHb: deoxy-hemoglobin; tHb: total hemoglobin; OGTT 0: baseline (fasting) blood glucose concentration during the oral glucose tolerance test; TSI: tissue saturation index.

with GDM who exhibited lower exercise tolerance than women with uncomplicated pregnancies [11]. The lower skeletal muscle oxygen consumption and microvascular dysfunction (blunted microvascular reactivity) possibly contributed to these dysfunctions. Equally with muscle oxygenation, cerebral oxygenation, also significantly impaired in T1DM and T2DM [22,23], was observed as well in GDM patients [12].

Concerning macrovascular assessment, several studies have suggested that cIMT is significantly elevated in women with GDM compared with healthy ones [24,25]. A recent study has demonstrated that in uncomplicated first pregnancies, cIMT values remained increased even at 2 years post-partum and that these increased values may persist and promote long-term CVD risk [26]. In this case, similarly with brain and muscle oxygenation indices of macrovascular function were not significantly changed in the post-partum period.

Furthermore, rheocardiography has been proven a reliable, non-invasive method for the assessment of changes in cardiac output and ideal for repeated measurements in studies regarding the hemodynamic outcomes of a physiological or pharmacological intervention [27]. Cardiovascular function during the first trimester of pregnancy was observed to be different between uncomplicated pregnancies and those bound to develop gestational hypertensive disorders [28]. Similarly, pregnancies complicated by GDM, have been associated with increased left ventricular (LV) mass, impaired LV relaxation and lower LV systolic function, indicators of early diabetic cardiomyopathy capable of progressing to overt heart failure in the future [29]. In this study, participants, once again, did not present significant changes in REO values obtained during pregnancy and post-partum.

Alterations in certain hematological parameters, focusing on platelet indices, have been associated with microvascular complications present in DM [30]. Study participants presented minor changes in most parameters assessed. Nevertheless, there was a significant increase in Ht, Hb and total platelet count. While OGTT values were improved post-partum, the same did not apply for glucose and HOMA-IR values and one participant was diagnosed with T2DM, one year following labor. Indeed, existing literature suggests that a previous diagnosis of GDM holds an estimated risk of up to 60% for developing T2DM in later life [31].

It is widely accepted that a higher prevalence of GDM is attributed to a higher BMI; thus, attempts are made towards lowering pre-pregnancy BMI through dietary intervention and exercise [32]. In the current study, both median weight and BMI values were improved post-partum, once again not in a significant manner. Possibly, the failure of these women to reduce their weight after delivery contribute to the non-significant differences in their vascular function. Obesity is also characterized by an impaired endothelial-mediated vasodilator response to increased blood flow, to insulin and to biochemical agents [33]. Indeed, the findings of a previous study demonstrated significant microvascular and oxygenation differences between groups following adjustment for BMI differences [11].

We also attempted to identify correlation between OGGT glucose at time 0 min and skeletal muscle oxygenation as well as cerebral oxygenation parameters. A previous study detected significant correlation between NIRS variables during a circulatory occlusion maneuver (i.e. examining indices of microvascular reactivity) assessed at 28 ± 2 weeks with OGTT values (assessed four weeks earlier, before the initiation of GDM treatment), as well as with indices of arterial stiffness [11]. Although in this study no significant correlation was observed between the exercise NIRS measurements and OGTT values, the circulatory occlusion reperfusion data were not examined. Future studies are needed to assess whether vascular reactivity measurements are improved post-partum.

Limitations

The present study possesses considerable strengths, including prospective study design and detailed and precise statistical analysis. Nevertheless, we must acknowledge several limitations. First, the sample size was considerably small, since we had to re-assess the same women we assessed during pregnancy, having completed one year following delivery. In addition, the study did not involve a control group. However, current study findings combined with previous research suggest that both vascular lesions and impaired tissue oxygenation remain even in cases where the glycemic profile is improved post-partum.

Future perspectives

Regardless of the precise methodology and the extent of diagnostic parameters assessed in this study, there is certainly room for future research. This study has to be considered as a pilot one that will motivate further research with larger study samples. Larger size samples are needed to detect possible changes in additional parameters and investigate a possible lower post-partum exercise tolerance in these women. Thus, future studies will be able to arrive at robust conclusions regarding the improvement of both muscle and cerebral oxygenation in women with GDM-complicated pregnancies.

Conclusions

To our knowledge, for the first time, we provided evidence that in women diagnosed with GDM, although several hematological parameters observed during pregnancy were significantly improved post-partum, the same did not apply for vascular and muscle/cerebral oxygenation parameters. With the implementation of non-invasive NIRS, we managed to record the muscle and brain parameters at the same time. More studies are needed to provide data regarding muscle and cerebral oxygenation in GDM-complicated pregnancies as well as the association between glucose concentrations and skeletal muscle/cerebral oxygenation parameters.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

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