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Depressive symptoms, impaired glucose metabolism, high visceral fat, and high systolic blood pressure in a subgroup of women with recent gestational diabetes

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ABSTRACT

Women with gestational diabetes (GDM) are a high risk group for early type 2 diabetes (T2D). Depression is a risk factor for T2D in the general population. We investigated in women after a recent pregnancy with GDM and without a clinical diagnosis of depression, whether mild to moderate depressive symptoms associate with pathologic glucose metabolism. In a cross-sectional analysis, we examined 173 women, 9 ± 3 months after delivery with several psychopathological assessments, 5-point oral glucose tolerance test with insulin, anthropometrics, and laboratory chemistry. In a subgroup of 101 women, abdominal visceral fat was quantified by magnetic resonance imaging (MRI).

A total of 22 women (13%) showed mild to moderate depressive symptoms, and the proportion of women with pathologic glucose metabolism (impaired fasting glucose, impaired glucose tolerance, or T2D) was higher in this group than in the women without depressive symptoms (59.1% vs. 33.1%, p = 0.018). Women with depressive symptoms also had higher body mass index (BMI), systolic blood pressure, plasma leptin, plasma resistin, and abdominal visceral fat volume. Pathologic glucose metabolism (OR = 2.594, 95% CI: 1.021–6.592), systolic blood pressure (OR = 1.076, 95% CI: 1.027–1.128), and abdominal visceral fat volume (OR = 2.491, 95% CI: 1.142–5.433) remained, even after adjustment for BMI, associated with the presence of depressive symptoms.

Taken together, we found depressive symptoms at a level not generally diagnosed in clinical practice in a subgroup of women with recent GDM. This subgroup also showed an unfavorable metabolic profile. Mild to moderate depressive symptoms may therefore help to identify this special subgroup.

1. Introduction

Depression and type 2 diabetes mellitus (T2D) interact bidirectionally (Lustman and Clouse, 2007; Renn et al., 2011). Depression increases the risk of T2D by 37% (Knol et al., 2006), while individuals suffering from T2D have a doubled risk of developing depression (Anderson et al., 2001).

Depression also impairs the treatment success of T2D because it hinders compliant behavior and increases cortisol release, which in turn raises plasma glucose (Lustman et al., 2000); (Lustman and Clouse, 2005). Additionally, many antidepressants can lead to weight gain (Barnard et al., 2013). On the other hand, treatment with antidepressants may improve glycemic control in parallel with the improvement in psychopathology (Lustman and Clouse, 2005 and 2007).

Gestational diabetes (GDM) is a transient disturbance of glucose metabolism that currently occurs in 6–8% of pregnancies in Germany (Tamayo et al., 2016). It can lead to macrosomia and other neonatal complications and is a strong risk marker for early (permanent) T2D in the mother. About 20–70% of GDM women developed T2D in a 10-year follow up and numbers are rising (Kim et al., 2002); (Bellamy et al.,

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Abbreviations

hsCRP	high sensitivity c-reactive protein
ISI	insulin sensitivity index
T2D	type 2 diabetes mellitus
VO2peak	peak volume of oxygen uptake
GDM	gestational diabetes mellitus
NEFA	non-esterified fatty acids
NGT	normal glucose tolerance
PGT	pathological glucose tolerance
BMI	body mass index
HDL	high density lipoprotein
OGTT	oral glucose tolerance test
BIA	bioelectrical impedance analysis

2009). Decreased beta-cell function and insulin sensitivity are suggested to be associated with biomarkers such as leptin, adiponectin, resistin, or changes in non-esterified fatty acids (NEFA) (Rottenkolber et al., 2015); (Fugmann et al., 2015). Additionally, these biomarkers show distinct changes in psychiatric disorders such as major depression (Jow et al., 2006; Lehto et al., 2010). An interaction between leptinergic and serotonergic systems in the central nervous system has been described by (Leibowitz and Alexander, 1998).

Depressive symptoms early in pregnancy have been linked to the later development of GDM and GDM, in turn, to the risk of postpartum depression. We investigate whether psychological impairments in patients not obviously suffering from postpartum depression and after remission of GDM in the postpartum care could be linked to an elevated risk for metabolic changes in these patients.

2. Individuals and methods

2.1. Study population

Women enrolled in the presented analysis were probands of the prospective monocenter observational study PPSDiab ("**P**rediction, **P**revention and **S**ub-classification of type 2 **Diab**etes"), which recruited from November 2011 until May 2016. The study population consisted of women who had a recent pregnancy. The cohort was recruited consecutively from the Diabetes Center and the obstetrics department of the University Hospital (Klinikum der Universität München) in Munich, Germany. Women were included within 15 months after delivery.

Exclusion criteria for this study were alcohol or substance abuse, pre-pregnancy diabetes, (post)menopausal status, or chronic diseases requiring systemic medication (except for hypothyroidism (n = 52), mild hypertension (n = 4), gastroesophageal reflux (n = 2), history of pulmonary embolism resulting in Rivaroxaban prophylaxis (n = 1), bronchial asthma (n = 8)).

For this subgroup analysis, women at high risk of T2D as GDM during their last pregnancy were included. Diagnosis of GDM was based on an oral glucose tolerance test (OGTT) following the criteria of the International Association of Diabetes and Pregnancy Study Groups (IADPSG). For detailed study criteria, please see Ferrari et al. (2015) (Ferrari et al., 2015).

Written informed consent was obtained from all study participants, and the protocol was approved by the ethics review committee of the Ludwig-Maximilians-Universität.

All data used in this analysis were collected at the baseline visit, 3–16 months after the index pregnancy.

2.2. Medical documentation and oral glucose tolerance test

At the first postpartum visit, detailed medical history was recorded and physical examination was conducted, including body weight and body fat mass. Body mass index (BMI) was calculated as weight in kilograms divided by height squared in meters.

All participants underwent a 5-point 75 g OGTT with measurement of plasma glucose and serum insulin after an overnight fast and were divided into normoglycemic subjects (NGT: fasting plasma glucose < 100 mg/dl and 2 h plasma glucose < 140 mg/dl) and subjects with pathological glucose tolerance (PGT: fasting plasma glucose ≥100 mg/dl and/or 2 h plasma glucose ≥140 mg/dl). The OGTT data were also used to calculate the insulin sensitivity index (ISI) according to Matsuda and De Fronzo (Matsuda and DeFronzo, 1999).

During the OGTT, blood pressure was obtained from all subjects in a seated position after at least 15 min of rest, on both arms, with repeated measurement on the arm with the higher systolic value. The mean of the two measurements was recorded.

2.3. Questionnaires

Composite International Diagnostic Interview (CIDI), which is a standardized, clinically structured interview that enables the diagnosis of mental disorders based on DSM and ICD criteria (Maske et al., 2015), was used for validation in the first 100 patients for exclusion of psychiatric disorders as influencing factors.

The Beck Depression Inventory (BDI) I (16%) and II (84%) (Beck, 1961) (Beck et al., 1996); were used to assess depressive symptoms. This is a 21-question multiple-choice questionnaire for individuals aged 13 years and older with items related to depressive symptoms (e.g., hopelessness, irritability), cognitions (e.g., guilt, feelings of being punished), and physical symptoms (e.g., fatigue, weight loss). Scores are ranked as follows: no depression (BDI I: 0–9; BDI II: 0–13), mild depression (BDI I: 10–18; BDI II: 14–19), moderate depression (BDI I: 19–29; BDI II: 20–28), and severe depression (BDI I: 30–63; BDI II: 29–63).

Further questionnaires used were the following as described in Ferrari et al., 2015): Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), Perceived Stress Scale (PSS) (Cohen et al., 1983), and furthermore the State-Trait Anxiety Inventory (STAI) for evaluation of anxiety affect (Spielberger CD, Gorsuch RL, Lushene RE. Manual for the state-trait anxiety inventory, 1970) differentiated for state (STAIX1) and trait (STAIX2) anxiety (Cattell and Scheier, 1961).

2.4. Laboratory methods

Blood samples were processed immediately. Collected plasma samples were stored at −80 °C until assayed.

The following laboratory parameters were analyzed: glucose, insulin, HbA1c, high sensitivity c-reactive protein (hsCRP), high density lipoprotein (HDL)-cholesterol. Total NEFA concentration was determined by enzymatic calorimetric method (NEFA Kit, Wako Chemicals, Neuss, Germany).

2.5. Fitness parameter

For determination of the fitness cardiopulmonary exercise testing was performed on a bicycle ergometer using the spiroergometry system MasterScreen CPX (Care Fusion, Höchberg, Germany) as described previously (Gar et al., 2017).

The peak oxygen uptake (VO2peak) is a close approximation of VO2max (Day et al., 1985). 142 probands accomplished the exercise test for inclusion in the analysis.