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ORIGINAL ARTICLE

Postpartum adiponectin changes in women with gestational diabetes

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Abstract

Introduction and objective. Current literature provides contradictory information on the role of adiponectin (AdipoQ) in the course of gestational diabetes mellitus (GDM) and the changes after delivery. The aim of the study was to measure AdipoQ concentration in blood of women with GDM, and to conduct a comparative analysis of AdipoQ concentrations in gestation at 3 and 12 months after delivery.

Material and methods. The study group consisted of 50 women diagnosed with GDM between 24 and 28 weeks of gestation. Three months after delivery, 41 women underwent further tests, while 12 months after delivery 30 patients. All patients underwent clinical and laboratory evaluation at GDM diagnosis at 3 and 12 months after delivery. Laboratory evaluation included fasting glucose, fasting insulin, OGTT and lipid parameters in serum. Serum AdipoQ concentration was measured at GDM diagnosis as well as at 3 and 12 months after delivery.

Results. AdipoQ concentrations did not differ significantly between the groups during gestation ($p=0.7054$) and 3 months after delivery ($p=0.9732$), while a significant rise was observed 12 months after delivery, compared to the values during pregnancy ($p=0.0006$). AdipoQ in the GDM group 12 months after delivery inversely correlated with fasting glucose and 2-hour post-load plasma glucose after a 75-g oral glucose tolerance test ($r=-0.37^{*}$; $p<0.05$ and $r=-0.42$, $p<0.05$, respectively).

Conclusions. An increased level of AdipoQ after delivery in the comparison to women with GDM may be a marker for reversibility of carbohydrate metabolism disorders, while a negative correlation between AdipoQ and glucose levels suggests that this parameter may be a predictor In the future of disturbances in glucose tolerance in women with GDM.

Key words

adiponectin, gestational diabetes, insulin resistance, pospartum changes

INTRODUCTION

Gestational diabetes mellitus (GDM), defined as a carbohydrate intolerance of varying severity with onset or first recognition during pregnancy, is a common complication of gestation [1]. Current data indicate that GDM is associated with an increased risk of complications for both the mother and the child during pregnancy and birth [2]. Furthermore, it is believed that GDM is a slow developing form of type 2 diabetes (T2DM) in the stage of increasing insulin resistance, which arises from the hormonal activity of the placenta, and remains a T2DM risk factor for the mother in the future [3]. Several studies have demonstrated evidence of the increased cardiovascular risk and higher prevalence of cardiovascular events later in life in the population of women with previous GDM [4, 5, 6]. The pathogenesis of GDM is multifactorial and may include genetic and environmental factors which are not yet been fully understood. The well-known hallmarks of human pregnancy are insulin resistance and increased adiposity, phenomena which lead scientists to seek for new biomarkers of GDM and future cardiovascular risk [7].

In recent years, adiponectin (AdipoQ), the main adipokine of adipose tissue, has been linked with insulin sensitivity and its regulation in tissues [7, 8]. Low AdipoQ in serum has been reported to correlate with insulin-resistant phenotype, obesity and development of metabolic and cardiovascular disorders [9]. The data on AdipoQ concentration in GDM are contradictory [10]. Retnakaran et al. have shown a decline in its concentration, accompanied by increased insulin resistance during gestation, which would corroborate the fact that this cytokine participates in the pathogenesis of insulin resistance [11]. However, studies by other researchers, e.g. Thyfault et al., demonstrate that the concentration of AdipoQ may depend on the severity of insulin resistance and carbohydrate metabolism disorders [12]. In a previous study we observed that AdipoQ concentration in serum of women with GDM does not differ from the level in healthy pregnant subjects, which may be explained by early diagnosis and prompt treatment [13]. Little is known about adiponectin changes after delivery and its role in prediction of future diabetes and increased cardiovascular risk. Therefore, the aim of the presented study was to measure AdipoQ concentration in blood of women with GDM, and to conduct a comparative analysis of AdipoQ concentrations in gestation at 3 and 12 months after delivery.

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MATERIALS AND METHOD

Patients. The study was conducted on pregnant women from the Lublin region in southeast Poland who underwent routine prenatal tests for GDM in compliance with the guidelines of the Polish Diabetes Association [1]. The study group consisted of 50 women diagnosed with GDM between 24 and 28 weeks of gestation. A 75-gram glucose oral glucose tolerance test (OGTT) was used for the diagnosis of GDM. It was diagnosed if one or two plasma glucose levels met or exceeded the following thresholds: fasting glucose concentration of 100 mg/dl and/or 2-hour glucose concentration of 140 mg/dl. The control group comprised 21 healthy pregnant women with normal OGTT results. Three months after delivery, 41 women underwent further tests, while 12 months after delivery, 30 patients were tested (82% and 60%, respectively). The patients enrolled into the study provided written informed consent to participate and filled out a questionnaire which included the following information: patient's age, height, pregestational weight, medical, family and obstetric history. The study protocol was accepted by the Bioethics Committee of the Medical University in Lublin.

Study design. All patients underwent clinical and laboratory evaluation at GDM diagnosis, i.e. between 24 and 28 weeks of gestation at 3 and 12 months after delivery. Anthropometric measurements were obtained from all participants. Weight was taken in light clothes and height without shoes. Body mass index was calculated according to the formula: weight (kg)/height (m^2). Additionally, a retrospective analysis of anthropometric measurements was performed before gestation. Laboratory evaluation at GDM diagnosis included routine laboratory tests (fasting glucose, fasting insulin, total cholesterol, HDL cholesterol and triglycerides in serum). AdipoQ concentration was measured in serum at GDM diagnosis, as well as at 3 and 12 months after delivery. At the last two points of time, the women had their carbohydrate metabolism tested with the use of the OGTT; insulin and cholesterol fractions were also assayed.

Methods. The assays were performed with the use of a routine laboratory method with a biochemical analyzer ADVIA 1650 with Siemens'Advia Chemistry reagent sets. The atherogenic index was calculated based on the concentration of triglycerides and HDL cholesterol [14]. The index above 0.5 indicated an increased risk of cardiovascular complications. The LDL cholesterol concentration was calculated with the Friedewald equation [15]. Additionally, the indirect index of insulin resistance – HOMA–IR (Homeostasis Model Assessment – Insulin Resistance) was calculated [16]. Serum AdipoQ concentrations were measured with a commercial enzyme-linked immunosorbent assay kit: 'Adiponectin Human ELISA', Catalogue No.: RD195023100, obtained from BioVendor Laboratory Medicine (Modrice, Czech Republic), according to manufacturer's instructions. The limit of detection was 26 ng/mL. The intra- and inter-assay coefficients of variation (CVs) were 4.9% and 6.7%, respectively. The results were read on a microtiter plate reader ELx 800 (Bio-Tek Co Ltd, USA). Laboratory analyses were carried out in the Central Laboratory of Clinical Hospital No. 4 (SPSK4) and the Department of Laboratory Diagnostics of the Medical University in Lublin, Poland.

Statistical analysis. Fisher's exact test and Mann–Whitney test were employed to compare proportions and quantitative variables, respectively. Wilcoxon signed-rank test was used to evaluate the adiponectin concentration during gestation and after delivery. Partial Spearman correlation coefficients between AdipoQ serum concentrations and other laboratory parameters were calculated. The results are expressed as median (interquartile range). All tests were considered significant with $p<0.05$. All analyses were performed with the MedCalc ver. 11.4.3.0.

RESULTS

Clinical characteristics of the study group. Table 1. shows the clinical characteristics of the study group. No significant differences were found between the groups in terms of the patients'weight and BMI before and during pregnancy, i.e. at GDM diagnosis. What is more, the weight and BMI of women with GDM measured 3 months after delivery, compared to their respective values during gestation, were similar, although they were significantly higher than the pregestational values. The studied parameters evaluated 12 months after delivery were significantly lower than those during gestation and 3 months after delivery, but they did not differ significantly compared to their respective pregestational values.

Table 1. Clinical characteristics of the study group

Studied parameter		Study group
Age (years)		31.0 (29.0–32.0)
Height (m)		1.63 (1.6–1.67)
Weight (kg)	before gestation	61.5 (58.0–66.0)
	during gestation	71.0 (66.7–75.0)
	3 months after delivery	70.0 (65.0–72.2)*#
	12 months after delivery	62.0 (60.0–70.0)*#
BMI (kg/m^2)	before gestation	23.0 (21.6–25.8)
	during gestation	26.9 (24.8–30.0)
	3 months after delivery	25.9 (23.9–27.8)*#
	12 months after delivery	23.2 (22.0–27.5)*#
Pregnancy	first	20 (40%)
	second	19 (38%)
	third and subsequent	11 (22%)
Birth weight (g)		3205.0 (3100.0–3650.0)
Gestational age (weeks)		26.0 (25.0–28.0)
History of miscarriage	no	31 (62%)
	one	15 (30%)
	two	4 (8%)
History of GDM	no	43 (86%)
	yes	7 (14%)
Family history of diabetes	no	22 (44%)
	yes	28 (56%)

Quantitative variables – median (interquartile range)
Qualitative variables – number of observations (percentage)
* $p < 0.05$ compared with values during gestation
# $p < 0.05$ compared with values before gestation

Evaluation of metabolic parameters in the GDM group. Evaluation of glycaemia, insulin resistance and lipids in the

study group during gestation and after delivery is shown in Table 2. Three and 12 months after delivery the above parameters were significantly lower than their respective values between 24 and 28 weeks of gestation. Moreover, glucose in the 75g 2h OGTT was significantly lower after delivery than during gestation. Three and 12 months after delivery, the studied lipid parameters in the GDM group were significantly depressed, compared with their values during pregnancy. Only the HDL cholesterol concentrations did not differ.

Table 2. Evaluation of metabolic parameters in the study group during gestation and after delivery

Studied parameter		Study group during weeks 24–28 of gestation	Study group 3 months after delivery	Study group 12 months after delivery
Fasting glucose (mg/dl)		87.0 (79.0–93.0)	81.0 (76.0–88.0)	80.0 (76.0–88.0)*
Fasting insulin (mU/l)		10.9 (7.0–15.0)	5.5 (4.5–6.7)*	4.5 (4.1–5.9)*
HOMA-IR		2.4 (1.9–3.5)	1.1 (0.9–1.3)*	0.9 (0.8–1.2)*
glucose in OGTT (mg/dl)	0 min.	87.0 (79.0–93.0)	81.0 (76.0–88.0)*	80.0 (76.0–88.0)*
	120 min.	167.0 (156.0–189.0)	104.0 (98.0–115.0)*	110.5 (98.0–115.0)*
Cholesterol (mg/dl)		268.0 (250.0–289.0)	220.0 (204.0–236.5)*	199.0 (190.0–210.0)*
LDL cholesterol (mg/dl)		150.1 (134.6–165.0)	122.0 (111.75–134.0)*	100.0 (96.0–110.0)*
HDL cholesterol (mg/dl)		70.1 (65.0–76.0)	72.1 (67.15–77.175)	71.0 (66.0–76.0)
Triglycerides (mg/dl)		245.0 (223.0–268.0)	161.5 (145.0–170.0)*	112.0 (110.0–125.5)*
Atherogenic index		0.536 (0.506–0.595)	0.342 (0.293–0.392)*	0.212 (0.168–0.266)*
Adiponectin (μg/ml)		15.8 (12.8–17.8)	14.9 (13.8–16.0)	18.9 (16.8–21.9)*

Quantitative variables – median (interquartile range)
* $p < 0.05$ compared with values during gestation

Evaluation of adiponectin concentration in the GDM group. No significant changes were observed in the concentration of AdipoQ in the study group 3 months after delivery, while a significant rise was observed 12 months after delivery, compared to the values during pregnancy and 3 months after delivery.

Evaluation of correlations between adiponectin concentration and clinical features in the GDM group. Table 3 shows adiponectin relations between concentration and the studied parameters in the study group during gestation and after delivery. In the GDM group, during pregnancy and 3 months after delivery, no significant correlations were observed between the concentration of AdipoQ and glycaemia and HOMA-IR values. Only 12 months after delivery negative correlations between AdipoQ concentration and fasting glucose and in the 75g 2h OGTT were found. No differences were detected between the studied adipokine and the lipid parameters.

Table 3. Evaluation of correlations between adiponectin concentration and metabolic parameters in the study group during gestation and after delivery

Studied parameter		Study group during weeks 24–28 of gestation	Study group 3 months after delivery	Study group 12 months after delivery
Fasting glucose (mg/dl)		0.0648	–0.168	–0.37*
Fasting insulin (mU/l)		–0.0534	–0.0479	–0.0546
HOMA-IR		0.0533	–0.0966	–0.182
glucose in OGTT (mg/dl)	0 min.	0.0648	–0.168	–0.37*
	120 min.	–0.0404	–0.0907	–0.42*
Cholesterol (mg/dl)		–0.124	0.0644	–0.196
LDL cholesterol (mg/dl)		–0.12	0.0321	0.0636
HDL cholesterol (mg/dl)		–0.0503	0.0259	0.228
Triglycerides (mg/dl)		–0.0541	0.0469	–0.152
Atherogenic index		–0.0193	–0.0238	–0.256

* $p < 0.05$ in the Spearman's rank correlation

DISCUSSION

Evaluation of AdipoQ level in GDM patients and after delivery may serve as a potential source of information about the development of metabolic disorders, and may also be of prognostic value. Current literature provides little and contradictory data on the role of AdipoQ in the course of GDM and the changes after delivery. To date, pathophysiological implications of AdipoQ have been rather poorly explained, even though many authors have emphasized the multidirectional role of this adipokine in obesity, T2DM, metabolic syndrome or GDM, especially the link between adiponectinemia and those disorders[17, 18, 19].

The fundamental aspect of the presented study was to analyze AdipoQ concentration over time, starting from the second trimester of gestation (between 24 – 28 weeks) and then at 3 and 12 months after delivery. The period of 3 months was selected following the findings in literature that have shown that metabolic disorders typical for pregnancy subside between 8 – 12 weeks after delivery. At this point in time, re-examination of carbohydrate metabolism is recommended [20]. The tests performed 3 months after delivery showed a marked decline in insulin resistance parameters and improved metabolism, compared with the period of gestation. Despite the improved metabolic parameters, however, the concentration of AdipoQ did not change compared to the period of gestation. This is analogous to the results of the Australian authors [21]. Liu T at al. who showed that the levels of adiponectin at day 3 and day 42 in the study group did not differ significantly compared to the period of pregnancy [22]. It should be stressed that in a further 12 month-long observation, we found a significant rise in AdipoQ concentration with accompanying weight loss, although with no significant changes in insulin resistance parameters were noted compared to 3 months after delivery. A negative correlation, known among researchers but not shown in the presented study, between AdipoQ concentration and weight, clearly explains the observed dependence of these parameters, both in gestation and after delivery [23, 24, 25]. Esposito et al. showed a marked increase of AdipoQ concentration in obese premenopausal women following

weight loss during a 2-year-long observation based on diet and lifestyle modifications [26], whereas Abbasi et al. demonstrated that the AdipoQ level does not change as a result of reduced weight within a short 3–4-month-long observation. This may indirectly suggest that time is an important factor in modifying this parameter [27].

The rise in AdipoQ concentration 12 months after delivery should be emphasized as this value reached significance, not only when compared with the early post-delivery period, but also with the time of gestation. Such a dynamic change in the AdipoQ level may imply reversibility of some metabolic disorders induced by pregnancy.

Attention should be paid to the negative correlation between AdipoQ concentration and glucose tested while fasting and after glucose load in the OGTT 12 months after delivery, which may suggest that this parameter could be a potential predictor in the prevalence of post-delivery glucose intolerance in patients with previous GDM. It is a well-established fact that this population has high risk for T2DM development and is an object of multidirectional studies aimed at finding an important predictor of this disease [11, 28, 29]. Schaefer-Graf et al. have already placed fasting glucose among the most important predictive factors for glucose intolerance after delivery [28]

In the light of contradictory findings about the role of AdipoQ in GDM and the fact that this parameter may be a predictor of impaired glucose tolerance in women with previous GDM, there is a need for further and more detailed research in this field. It is necessary to find important mediators which play a role in insulin resistance pathogenesis, the analysis of which would allow us to comprehend the nature of the disorders underlying GDM.

CONCLUSIONS

Based on the conducted study, it may be concluded that an increased level of AdipoQ after delivery may be a marker for reversibility of carbohydrate metabolism disorders, while a negative correlation between AdipoQ and glucose levels suggests that this parameter may be a future and important predictor of impaired glucose tolerance in women with GDM.

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