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ORIGINAL ARTICLE

Unfavorable cytokine and adhesion molecule profiles during and after pregnancy, in women with gestational diabetes mellitus

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KEYWORDS
Metabolic syndrome;
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Postpartum

Abstract
Background: Gestational diabetes mellitus is a significant risk factor for metabolic syndrome and cardiovascular disease.
Aims: To assess the relationships between components of the metabolic syndrome and cytokine and adhesion molecule levels in women with GDM during pregnancy and after delivery.
Patients and methods: A prospective case–control study on a sample of 126 pregnant women (63 with and 63 without gestational diabetes mellitus). In an intra-subject analysis, 41 women with history of gestational diabetes mellitus and 21 controls were re-assessed in the postpartum period. Clinical data and levels of cytokines and adhesion molecules were recorded during weeks 24–29 of pregnancy and 12 months after delivery.

Abbreviations: AMs, cell adhesion molecules; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; E-selectin, cellular molecule; GDM, gestational diabetes mellitus; HDL, low high-density lipoprotein; ICAM-1, intercellular adhesion molecule-1; IL-6, interleukin 6; IR, insulin resistance; MetS, metabolic syndrome; OGTT, oral glucose tolerance test; OR, odds ratio; SD, standard deviation; SE, standard error; TNF-α, tumor necrosis factor alpha; T2DM, type 2 diabetes mellitus; VCAM-1, vascular adhesion molecule-1; WC, waist circumference.

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Results: In the postpartum period, there were significantly higher levels of tumor necrosis factor alpha in both cases and controls, and of adiponectin in controls. Cases showed higher leptin levels, with no significant differences during and after pregnancy. No significant differences were seen in adhesion molecules and interleukin-6 between cases and controls during pregnancy and in the postpartum period, but levels of both were higher in cases. During pregnancy and after delivery, adiponectin decreased in cases and increased in controls. Significant positive correlations were seen between adiponectin and fasting blood glucose levels and vascular cell adhesion molecule-1, and also between leptin and tumor necrosis factor alpha levels.
Conclusions: The results suggest that increased inflammation and transient hyperglycemia during pregnancy would represent a latent form of metabolic syndrome, with an increased risk for type 2 diabetes mellitus and future cardiovascular disease.

PALABRAS CLAVE
Síndrome metabólico;
Adipocinas;
Disfunción endotelial;
Diabetes mellitus gestacional;
Posparto

Perfiles de citocinas y moléculas de adhesión desfavorables durante y después del embarazo en mujeres con diabetes mellitus gestacional

Resumen
Antecedentes: La diabetes mellitus gestacional es un factor de riesgo importante para el síndrome metabólico y la enfermedad cardiovascular.
Objetivos: Se evaluaron las relaciones entre los componentes del síndrome metabólico, los niveles de citocinas y moléculas de adhesión en mujeres con diabetes gestacional durante el embarazo y en el posparto.
Pacientes y métodos: Estudio prospectivo de casos y controles. Se analizaron 126 mujeres gestantes (63 con diabetes mellitus gestacional y 63 controles). En el periodo posparto, se reevaluaron 41 casos y 21 controles. Se analizaron variables clínicas, niveles de citocinas y moléculas de adhesión durante las semanas 24-29 de la gestación y 12 meses después del parto.
Resultados: En el periodo posparto, el factor de necrosis tumoral alfa en casos y controles, y la adiponectina en controles fueron significativamente más altos. Los casos mostraron mayores niveles de leptina, sin diferencias significativas durante el embarazo y después del parto. No se observaron diferencias significativas en las moléculas de adhesión y la interleucina 6 entre casos y controles durante el periodo de embarazo y el posparto, pero ambos fueron mayores en los casos. Durante el embarazo y posparto, la adiponectina disminuyó en los casos y aumentó en los controles. Observamos correlaciones positivas significativas entre adiponectina con glucemia en ayunas y moléculas de adhesión celular vascular-1, y entre leptina y factor de necrosis tumoral alfa.
Conclusiones: Los resultados indican que el aumento de la inflamación y la hiperglucemia transitoria durante el embarazo representarían una forma latente de síndrome metabólico, con un mayor riesgo de diabetes mellitus tipo 2 y de enfermedad cardiovascular en el futuro.

Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that begins, or is first recognized, during pregnancy. It complicates about 1–14% of all pregnancies worldwide. GDM mothers and their offspring are at increased risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD). However, the mechanisms underlying these processes are unclear.[1]

Metabolic syndrome (MetS) is the clustering of central-trunk obesity, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hypertension and dysglycemia. However, there is no consensus as to what defines MetS. Insulin resistance (IR) is proposed as the common link between the different manifestations of MetS and, as well, the cause of most of the associated abnormalities.[2]

Adipokines regulate glucose metabolism, insulin secretion and its activity, and fetal development. A high correlation between adiposity and IR with interleukin 6 (IL-6) concentrations has been described. High IL-6 secretion may aggravate IR in pregnancy and participate in the pathogenesis of GDM. Tumor necrosis factor alpha (TNF-α) has been used to predict GDM and its prognosis.[3] TNF-α and IL-6 are involved in mechanisms that contribute to endothelial damage, including inhibition of endothelial nitric oxide synthase, vascular smooth muscle proliferation, and elevated concentrations of adhesion molecules.[4] Pregnancy, such as obesity,