Psychoneuroendocrinology (2015) 51, 92—100

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Plasma adiponectin is inversely associated with antenatal anxiety: Results from a Brazilian cohort

Fernanda Rebelo[a,b], Thatiana de Jesus Pereira Pinto[b], Ana Beatriz Franco-Sena[b], Jaqueline Lepsch[b], Camila Benaim[b], Claudio José Struchiner[a], Gilberto Kac[b,*]

[a] National School of Public Health, Oswaldo Cruz Foundation, Rua Leopoldo Bulhões, 1480 Manguinhos, Rio de Janeiro, RJ, Brazil
[b] Nutritional Epidemiology Observatory, Department of Social and Applied Nutrition, Institute of Nutrition Josué de Castro. Rio de Janeiro Federal University, Avenida Carlos Chagas Filho, 367/CCS—Bloco J—2° andar, sala 29. Cidade Universitária—Ilha do Fundão, Rio de Janeiro, RJ, Brazil

Received 30 June 2014; received in revised form 14 August 2014; accepted 16 September 2014

KEYWORDS
Adiponectin;
Anxiety;
Mental health;
Pregnancy;
Cohort

Summary Antenatal anxiety may increase the risk of undesirable birth outcomes. Studies have demonstrated an association between adiponectin and anxiety, but this issue has not been investigated during pregnancy. This study aimed to evaluate the association between plasma adiponectin, measured throughout gestation, and the occurrence of anxiety at late pregnancy (30—36th weeks). A prospective cohort was investigated in Rio de Janeiro, Brazil. Healthy pregnant women, aged 20—40 years, were evaluated between gestational weeks 5—13, 22—26 and 30—36. State anxiety was measured using a validated version of the State-Trait Anxiety Inventory, and women were categorized as high (score ≥ 50, $n = 30$) or low anxiety (score < 50, $n = 129$). Plasma samples for all trimesters were analyzed using commercial ELISA kits to determine adiponectin concentrations (U/mL). Statistical analysis involved student's *t*-tests, chi-square, Pearson correlation, multiple logistic regression and linear mixed effects (LME) regression to model longitudinal trends of adiponectin, stratified for anxiety categories. Women with higher anxiety scores had lower mean concentrations of 3rd trimester adiponectin compared with those with lower scores (7.9; 95% CI: 7.0—8.9 *vs.* 9.9; 95% CI: 9.1—10.7). Women with 3rd trimester adiponectin values within the third tertile (10.47—26.57 U/mL) were less likely to have high antenatal anxiety (adjusted OR = 0.30; 95% CI: 0.09—0.98) compared

* Corresponding author at: Avenida Carlos Chagas Filho, 367, CCS, Bloco J/2, andar, sala 29, Cidade Universitária, Ilha do Fundão, Rio de Janeiro, RJ 21941-590, Brazil. Tel.: +55 21 39386595; fax: +55 21 22808343.
E-mail addresses: frebelos@gmail.com (F. Rebelo), thatiana.pinto@gmail.com (T. de Jesus Pereira Pinto), nutrianabeatriz@gmail.com (A.B. Franco-Sena), jaquelepsch@gmail.com (J. Lepsch), camilabenaimnutri@gmail.com (C. Benaim), stru@fiocruz.br (C.J. Struchiner), Gilberto.kac@gmail.com (G. Kac).

http://dx.doi.org/10.1016/j.psyneuen.2014.09.015

with those within the first tertile (2.25—7.08 U/mL). Unlike women with low levels of anxiety, those with high levels had a significant decrease of plasma adiponectin throughout pregnancy ($\beta = -0.07$; 95% CI: $-0.13 - [-0.01]$ *vs.* $\beta = -0.01$; 95% CI: -0.05 to 0.03). Multiple LME model indicated higher adiponectin throughout pregnancy for women with low anxiety ($\beta = -1.57$; 95% CI: $-2.78 - [-0.37]$). In conclusion, plasma adiponectin throughout pregnancy was inversely associated with antenatal anxiety.

1. Introduction

Studies conducted in pregnant women have shown that the prevalence of antenatal anxiety behaviors ranges from 6.6% to 19.8% (Andersson et al., 2003; Berle et al., 2005; Almeida et al., 2012; Rubertsson et al., 2014). Clinical anxiety, at this moment of life course, has been associated with adverse outcomes for the mother, such as increased risk of preeclampsia, greater frequency of nausea and vomiting during pregnancy, and occurrence of postpartum depression (Araújo et al., 2008; Qiu et al., 2009; Rubertsson et al., 2014). Anxiety symptoms may also have a negative impact on the development of the fetus and may increase the risk of low birth weight and preterm delivery (Van den Bergh and Marcoen, 2004; Li et al., 2008). Although anxiety during pregnancy is an important public health problem, this disorder has received little attention from health professionals and researchers.

Adiponectin is a hormone produced by adipocytes that sensitizes the body to insulin and that also has anti-inflammatory effects (Weyer et al., 2001; Fallo et al., 2004). Gustafson (2010) indicated the involvement of adiponectin in the inhibition of important pro-inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6, that have been positively associated with mental disorders (Gill et al., 2008). Previous studies have tested associations between adiponectin concentrations and mental health disorders such as anxiety and depression, but evidence of these associations remains inconsistent (Leo et al., 2006; Nagata and Yamada, 2006; Cizza et al., 2010; Diniz et al., 2012; Jeong et al., 2012; Wilhelm et al., 2013). Wilhelm et al. (2013) reported a positive correlation between adiponectin concentrations and anxiety in adults. However, Nagata and Yamada (2006) demonstrated that these variables were inversely correlated in women with eating disorders. Although the biological mechanisms involved in this association are not totally elucidated, some studies have suggested a strong contribution of the immune system and of metabolic factors (Cheng et al., 2012; Wang et al., 2014; Wilhelm et al., 2013).

This study aimed to evaluate the association between plasma adiponectin, measured longitudinally during gestation, and the occurrence of anxiety in late pregnancy. We sought to clarify the relationship between adiponectin concentrations and the occurrence of anxiety symptoms in pregnancy, during which time this behavioral disorder is associated with several adverse outcomes.

2. Methods

2.1. Study design and eligibility criteria

The present study comprised a prospective cohort design with pregnant women followed at Heitor Beltrão public health care center, located in the city of Rio de Janeiro, Brazil. The women were recruited between November 2009 and October 2011, and those who met the following eligibility criteria were invited to participate in the study: (a) in the 5th-13th week of gestation at the time of recruitment; (b) between 20 and 40 years of age; and (c) free of any chronic disease (other than obesity).

The cohort had three follow-up waves at gestational weeks 5—13, 20—26 and 30—36. Women were interviewed and blood samples were collected for subsequent laboratory analysis. The initial baseline sample comprised 299 pregnant women. However, we excluded women who presented twin pregnancies ($n = 4$), who were diagnosed with an infectious or non-communicable disease after entering the study ($n = 16$) or who had a miscarriage or stillbirth ($n = 27$). Of the remaining 252 women, we had 36 losses at follow-up due to transference of prenatal unit care ($n = 16$), change to an address out of the catchment area of the health unit ($n = 5$) or absence of the 3rd trimester interview ($n = 15$). Statistical analyses were performed to compare women lost with those who remained in the sample, with respect to socioeconomic, demographic, anthropometric and reproductive characteristics. There were no significant differences in any of these variables between the two groups of women (Supplemental file: Table S1).

After these exclusions and losses, the sample comprised 216 women. The analysis of adiponectin was only performed in a subsample of 171 women due to an operational problem experienced with the analysis procedure that caused the loss of two sets of data, one with 23 and the other with 22 samples. Finally, we decided to exclude outlying values (>30.0 U/mL; $n = 12$; range of excluded values 33.7—98.9), based on a normal adiponectin distribution proposed by Ahima (2006). Our final sample comprised 159 pregnant women.

2.2. Anxiety symptoms

The Spielberger State-Trait Anxiety Inventory (STAI) (Biaggio and Natalício, 1979) was used to measure anxiety symptoms during mid and late pregnancy (weeks 22—26 and 30—36, respectively). Although we have evaluated anxiety