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Thyroid function 48 h after delivery as a marker for subsequent postpartum depression

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Summary Physiological changes during gestation and after delivery are associated with postpartum thyroid dysfunction, which is due to thyroid autoimmunity in some cases. Postpartum thyroid dysfunction, in turn, has been associated with postpartum depression (PPD). The aim of the present study was to evaluate whether thyroid function immediately after delivery can predict postpartum depression at 8 weeks and 32 weeks after delivery. This study examined 1053 postpartum Spanish women without a previous history of depression. We evaluated depressive symptoms at 48 h, 8 weeks and 32 weeks postpartum and used a diagnostic interview to confirm major depression for all probable cases. Free thyroxin (fT4), thyroid-stimulating hormone (TSH), thyroid peroxidase antibodies (TPOAb) and C-reactive protein (CRP) were assayed at 48 h postpartum. Binary and multivariate logistic regression analyses were performed to determine independent risk factors for PPD.

Although 152 women (14.4%) had high TPOAb (>27 IU/mL) and slightly elevated TSH concentrations with normal fT4, we did not find any association between thyroid function and PPD. This thyroid dysfunction was not associated with CRP concentrations that were outside of the normal range (>3 mg/L). We conclude that thyroid function at 48 h after delivery does not predict PPD susceptibility.

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1. Introduction

Postpartum depression (PPD) affects approximately 13% of women (O'Hara, 1995; Garcia-Esteve et al., 2003), begins within the 6 months after childbirth and has a high economic impact on the family and on public health (Petrou et al., 2002).

The etiology of PPD is probably multifactorial, but thyroid dysfunction has been proposed as an etiologic factor for PPD (Harris, 1999). Postpartum changes in the immune system may be accompanied by increases in autoantibodies such as those against thyroid antigens. Postpartum thyroiditis (PPT), with a 5—7% prevalence (Muller et al., 2001), is a syndrome of transient or permanent thyroid dysfunction occurring in the first year after delivery due to autoimmune inflammation of the thyroid. Antibodies against thyroid peroxidase (TPOAb) are easy to measure and are used extensively as a marker for autoimmune thyroiditis (Sinclair, 2006). The presence of elevated concentrations of TPOAb concomitant with either thyroid dysfunction or euthyroid status has been associated with PPD (Harris et al., 1992; Kuijpens et al., 2001; McCoy et al., 2008). Other authors, however, have failed to find any relationship between PPD and PPT (Lazarus et al., 1997; Kent et al., 1999; Lucas et al., 2001; Oretti et al., 2003). On the other hand, immediate postpartum immune system activation has been demonstrated, for instance, by increased concentrations of IL-6 (Maes et al., 2002) and C-reactive protein (CRP) (De Meeus et al., 1998). Moreover, a meta-analysis by Howren et al. (2009) concluded that increased IL-1, IL-6 and CRP were positively associated with depression in clinical and community samples.

The aim of the present study was to evaluate whether thyroid function, TPOAb and CRP immediately after delivery (i.e., when the mother is at the maternity hospital) can predict postpartum depression at 8 weeks and 32 weeks after delivery.

2. Methods

2.1. Participants

Our sample was obtained from a larger multicenter study of postpartum depression conducted between December 2003 and October 2004 in Spain (Sanjuan et al., 2008). In the present study, we included 1053 of the 1804 postpartum women in the larger study, based on the additional requirement of available plasma and serum samples.

All participants were of Spanish family origin. Being under psychiatric care during pregnancy was an exclusion criterion. The ethics committees of the participating hospitals approved the study. Participants gave written consent after a full explanation and understanding of the study protocols. Participation consisted of a visit in an obstetric unit at 24—48 h postpartum for a semi-structured interview and tests (including a blood sample), at 8 weeks (coinciding with a standard postpartum obstetric clinic visit) and at 32 weeks (by phone and home visit) after delivery.

2.2. Assessment of depression

Depressive symptoms were assessed using the total score of the Spanish validated version of the Edinburgh Postpartum Depression Scale (EPDS) (Garcia-Esteve et al., 2003). EPDS was administered at baseline (24—48 h postpartum), 8 weeks and 32 weeks postpartum. All women who scored 9/10 in the EPDS at 8 weeks and 32 weeks postpartum were defined as probable cases of major depression. The cut-off of 9/10 for major depression maximizes the sensitivity to 100% and achieves a specificity of 89% (Navarro et al., 2007). All probable cases of major depression were evaluated using the Spanish version of the Diagnostic Interview for Genetics Studies (DIGS) for DSM-IV criteria (Roca et al., 2007) that we adapted for PPD. Trained clinical psychologists conducted all of the interviews. A high level of reliability ($K > 0.8$) was obtained among interviewers (Sanjuan et al., 2008). We used a case—control design to compare depressed women to non-depressed controls.

2.3. Blood sample and biochemical measurements

In the 48-h period after delivery, fasting blood samples were collected in 10 mL EDTA tubes and 5 mL anticoagulant-free tubes between 08:00 h and 09:00 h. The specimens were quickly centrifuged to separate out plasma and serum and were immediately frozen at $-80\,^{\circ}C$ until use. The entire batch of plasma and serum samples was analyzed simultaneously. Concentrations of free thyroxin (fT4), thyroid-stimulating hormone (TSH) and TPOAb were measured in serum using a microparticle enzyme immunoassay in an Axsym system (Abbott, Madrid, Spain). CRP was measured in plasma using an ultrasensitive turbidimetric immunoassay (CRP extended range) in a Dimension AR (Dade Behring, Barcelona, Spain). The sensitivity of the fT4 assay is 5.1 pmol/L, with a normal range of 9.13—23.80 pmol/L. TSH assay sensitivity is 0.03 μIU/mL, with a normal range of 0.49—4.67 μIU/mL. TPOAb assay sensitivity is 1 IU/mL, with a normal range of <12 IU/mL. The sensitivity of the CRP extended range assay is 0.5 mg/L, with expected values for healthy individuals of <3 mg/L.

We defined TPOAb as positive at or above a cut-off point of 27 IU/mL (the value of the third quartile in our entire sample). Thyroid dysfunction was identified if there was current hyperthyroidism (TSH < 0.49 μIU/mL and fT4 > 23.80 pmol/L), subclinical hyperthyroidism (TSH < 0.49 μIU/mL and normal fT4), hypothyroidism (TSH > 4.67 μIU/mL and fT4 < 9.13 pmol/L) or subclinical hypothyroidism (TSH > 4.67 μIU/mL with normal fT4). C-reactive protein was previously used as an inflammation marker (Pepys and Hirschfield, 2003) and has been related to depression (Howren et al., 2009) and thyroiditis (Pearce et al., 2003).

2.4. Statistical methods

Frequencies, which are provided as percentages, were used to describe qualitative variables (e.g., education level, marital and employment status, parity and thyroid dysfunction). We used mean and standard deviation (SD) to describe quantitative variables (e.g., age, TPOAb, fT4, TSH and CRP). TPOAb was categorized as positive (+) when the concentration of TPOAb was ≥27 IU/mL (representing the cut-off for the third quartile) and negative (−) when the concentration was <27 IU/mL. The non-parametric Mann—Whit-