Brief report

Thyroid function and postpartum mood disturbances in Greek women

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1. Introduction

Postpartum mood disturbances are very common in otherwise healthy women, and range from maternity blues, a mild phenomenon that is so common as to be regarded as normal, and has to be distinguished from the more serious postpartum depression (Pitt, 1973; Seyfried and Marcus, 2003; Gale and Harlow, 2003; Kemp et al., 2003). Rarely might in some cases occur postpartum psychosis (Seyfried and Marcus, 2003). A proportion of women with postpartum blues, if left unattended, may progress to overt postpartum depression (Kemp et al., 2003).

Thyroid function is known to be affected during pregnancy (Glinoer, 1997), while the pathogenesis of postpartum mood disturbances remains unclear. However, various investigators have attempted to establish a link between thyroid function, usually accompanied by autoimmune thyroiditis, with postpartum mood disorders (Harris et al., 1989; Pop et al., 1991; Hendrick et al., 1998). We have previously published that immune mechanisms may play a role in the etiopathology of postpartum depressive mood shifts (Boufidou et al., 2009). Furthermore, both hypothyroidism and hyperthyroidism, even if subclinical, may lead to depressive symptomatology (MacCrimmon et al., 1979; Kirkegaard and Faber, 1998).
This study aimed to investigate whether thyroid hormone levels in women free of overt or subclinical thyroid dysfunction may have an impact on the incidence of postpartum mood disturbances.

2. Patients and methods

2.1. Subjects

The study was conducted in Aretaieion University Hospital. Adult, native Greek, married women, with a gestational age of 35–38 weeks, free of obstetrical complications (preeclampsia, premature labor, instrumental delivery, and excessive bleeding intrapartum), thyroid disease, and eating disorders were invited to participate. Women with acute or chronic psychiatric disorders were excluded, to avoid misdiagnosing depression. Fifty-seven informed-consenting women completed the study. None of the women had complications after delivery and their hospital stay was 4–5 days. The study was approved by the Ethics Committee of the Aretaieion Hospital.

2.2. Study design

A detailed medical and obstetric history was recorded for each participant, which included parity, history of abortion or stillbirth, duration of menses and menstrual cycle, mode of previous delivery and breastfeeding. Weight was recorded on admission and daily until discharge. Additionally, blood samples were drawn on admission for delivery and daily until the fourth postpartum day. The obtained samples were immediately centrifuged and kept frozen at −80 °C till assayed.

2.3. Instruments

The psychological status of the participants was assessed using Greek versions of two systematically validated questionnaires.

1. The Postpartum Blues Questionnaire (P.B.Q.) (Kennerley and Gath, 1989), completed by mothers on admission and on days 1–4 postpartum.

2. The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987; Teissèdre and Chabrol, 2004; Muzik et al., 2000) was completed on day 4 and at 6 weeks postpartum (through a telephone interview).

2.4. Hormonal assays

Thyroid stimulating hormone (TSH, 2nd gen), free triiodothyronine (FT3), free thyroxin (FT4), anti-thyroglobulin antibodies (anti-TG) and anti-myeloperoxidase antibodies (anti-TPO) were measured with the Microparticle Enzyme Immunoassay kits: “TSH (2nd gen), Abbott Axsym”, “FT3, Abbott Axsym”, “FT4 Abbott Axsym”, “anti-TG Abbott Axsym” and “anti-TPO Abbott Axsym” respectively on Axsym® analyzer (Abbott Laboratories, USA).

2.5. Statistical analysis

We used STATA for the statistical analysis of the data. The cut-off score of the P.B.Q. was set to 8.2, which was the mean value of mean blues scores during the days 1–4 postpartum (Kennerley and Gath, 1989). The equivalent score of the EPDS was set to 11, after validation for the Greek population (Leonardou et al., 2009). Non-parametric tests were used in skewed data. We proceeded with comparison analysis and finally multiple regression analysis. The p-value ≤ 0.10 was used to indicate statistically significant results due to the small sample size and indicative nature of our study, while all possibly significant p-values are reported and p < 0.05 was regarded as the standard point of statistical significance.

3. Results

3.1. Exploratory data analysis

Characteristics of the subjects are summarized in Table 1.

3.2. Grouped (dichotomized) comparisons

Patients were divided according to their mood scores into two groups, high and low scoring, respectively, and the mean of thyroid measures, for baseline (before delivery) and final levels (postpartum) was compared. Regarding FT3, in baseline levels, the high scoring group had lower FT3 levels. Regarding FT4, in baseline and final levels, the high scoring group had lower FT4 levels. All possibly significant results corresponded in t-test and/or WMW (p-value ≤ 0.1) and were similar on the fact that lower FT3 or FT4 levels, higher TSH and anti-TPO antibodies levels associated with the high scoring group.

3.3. Correlation

We investigated possible correlations between test scoring and thyroid measures or other factors (pregnancy duration, duration of menstruation cycle, B.M.I., caesarian section), using Spearman’s (rho) correlation coefficient. Statistically significant results occurred at baseline levels, and specifically: Serum FT3 and FT4 correlated negatively with blues scores postpartum (blues on day 4, with FT3: rho = −0.44, p ≤ 0.01; with FT4, rho = −0.36, p ≤ 0.01) and with the mean blues score (with FT3, rho = −0.29, p ≤ 0.05; with FT4: rho = −0.3, p ≤ 0.05). Additionally, extension of pregnancy duration correlated negatively with mood scores, during the day 4 (rho = −0.34, p ≤ 0.05), as well as with the mean blues score (rho = −0.39, p ≤ 0.01). Caesarian section seemed to affect blues scores though not consistently (using the t-test, mean blues scoring was higher by 2.77 in women who underwent caesarotomy, p = 0.021), while it was not significantly associated to EPDS scoring at any period.

3.4. Regression

No significant difference was found between the blues scores during the first 4 days for each patient, so the regression analysis was performed in clusters (according to ANOVA). The mean postpartum blues score, treated as an overall measure, was analyzed separately. Showing significant difference over the two measurements (Wilcoxon signed-rank test for paired samples), the EPDS scores were separately analyzed. Antibody levels were not included in regression
analysis (missing values, problematic distribution of measurements). We proceeded with fitting multiple regression models, including the quadratic terms of thyroid hormones who reached statistical significance, as well as other reported factors. Regression models where adjusted according to pregnancy duration (more likely to present a confounding effect), while caesarian section was not included finally (not significant confounder in multiple regression analysis). Results are presented in Table 2.

Interestingly, baseline FT3 levels had a constant significant effect on postpartum blues levels (for days 1–4 and for the mean of the 4 days), and baseline FT4 levels had an almost significant effect on the mean score. Baseline and final FT4 levels had a quadratic effect on first week’s EPDS score and corresponded to a U-shaped curve of dependency of EPDS scores on FT4 levels (negative linear, positive quadratic coefficients).

4. Discussion

Following childbirth, women are vulnerable to the development of depression (Hendrick et al., 1998). Postpartum mood disorders seem to be relatively common among Greek women. The few existing studies demonstrate a prevalence of postpartum depression as high as 19.8%, while maternity blues occurs in approximately 44.5% of cases during the first days after delivery (Conidakis et al., 2008, 2007). The frequency of maternity blues is similar to the reported proportion from United States (O’Harra et al., 1991), France (Sutter et al., 1997) and Hong Kong (Hau and Levy, 2003).

On the other hand, the prevalence of thyroid dysfunction increases after childbirth as well (Hendrick et al., 1998). Postpartum thyroiditis is a recognized clinical entity, considered to be part of the spectrum of autoimmune thyroid disorders (Bloch et al., 2003; Stagnaro-Green, 2004). The condition is more frequently in women expressing thyroid antibodies early in pregnancy. (Stagnaro-Green, 2004).

Although depressive symptomatology is common in thyroid dysfunction, many studies trying to link postpartum mood disorders with thyroid dysfunction reported conflicting results (Bloch et al., 2003). Some reports suggested an association of postpartum depression with overt thyroid dysfunction (Harris et al., 1989; Pop et al., 1991) or with the mere presence of thyroid antibodies (Harris et al., 1992; Pop et al., 1993) even during early pregnancy (Kuijpers et al., 2001) Regarding TSH levels, George and Wilson (1983) found no association with early postpartum blues, while Pies (1997), reported opposite results. On the other hand, Okano (1989), found no significant correlation between thyroid function and maternity blues.

Some studies have focused on the association between thyroid hormone concentrations within the normal range

<table>
<thead>
<tr>
<th>Characteristic/factor</th>
<th>Mean</th>
<th>S.D.</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.69</td>
<td>4.29</td>
<td>22.00</td>
<td>45.00</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79.33</td>
<td>13.10</td>
<td>57.00</td>
<td>128.00</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.47</td>
<td>5.39</td>
<td>150.00</td>
<td>178.00</td>
<td></td>
</tr>
<tr>
<td>B.M.I. (kg/m²)</td>
<td>29.55</td>
<td>4.54</td>
<td>21.77</td>
<td>45.35</td>
<td></td>
</tr>
<tr>
<td>Menstruation duration</td>
<td>5.01</td>
<td>1.07</td>
<td>3.00</td>
<td>8.00</td>
<td></td>
</tr>
<tr>
<td>Menstruation cycle</td>
<td>28.44</td>
<td>3.05</td>
<td>22.00</td>
<td>39.00</td>
<td></td>
</tr>
<tr>
<td>Pregnancy duration</td>
<td>38.30</td>
<td>0.66</td>
<td>37.00</td>
<td>40.60</td>
<td></td>
</tr>
<tr>
<td>Gravidity (number of pregnancies)</td>
<td>2.21</td>
<td>1.36</td>
<td>1.00</td>
<td>9.00</td>
<td></td>
</tr>
<tr>
<td>Parity (number of births)</td>
<td>0.69</td>
<td>1.03</td>
<td>0.00</td>
<td>7.00</td>
<td></td>
</tr>
<tr>
<td>Been pregnant before</td>
<td>67.74%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given birth before</td>
<td>51.61%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>93.33%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caesarian section</td>
<td>70.97%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1

Reported characteristics/serum levels of women included in the study, according to patient files: mean value, standard deviation (S.D.), minimum and maximum values and proportion (%) recorded for each characteristic.

1B.M.I. = Body Mass Index.
2P.B.Q. = Postpartum Blues Questionnaire.
3EPDS = Edinburgh Postnatal Depression Scale.
Table 2

Multiple regression analysis of psychometric test scores (Blues = Postpartum Blues, EPDS = Edinburgh Postnatal Depression Scale) depending on thyroid-specific hormone levels, adjusting for pregnancy duration and investigating quadratic terms (included only if statistically significant).

<table>
<thead>
<tr>
<th>Test</th>
<th>Blues (days 1,2,3,4)</th>
<th>Mean Blues (days 1–4)</th>
<th>EPDS (first week)</th>
<th>EPDS (sixth week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free T3</td>
<td>−2.829 [−5.094, 0.346]</td>
<td>−2.859 [−5.752, 0.346]</td>
<td>−1.676 [−5.727, 2.375]</td>
<td>−2.508 [−5.828, 0.812]</td>
</tr>
<tr>
<td>(pg/ml)</td>
<td>(p = 0.016)</td>
<td>(p = 0.053)</td>
<td>(p = 0.409)</td>
<td>(p = 0.135)</td>
</tr>
<tr>
<td>Final</td>
<td>−0.608 [−3.189, 1.852]</td>
<td>−0.639 [−3.460, 1.852]</td>
<td>−1.429 [−5.245, 2.368]</td>
<td>−0.875 [−3.940, 2.190]</td>
</tr>
<tr>
<td>(ng/dl)</td>
<td>(p = 0.152)</td>
<td>(p = 0.106)</td>
<td>(p = 0.083)²</td>
<td>(p = 0.507)</td>
</tr>
<tr>
<td>TSH</td>
<td>0.417 [−0.728, 1.562]</td>
<td>0.239 [−1.137, 1.614]</td>
<td>Quadratic: 75.967 [−10.130, 162.065]</td>
<td>0.181 [−1.330, 1.692]</td>
</tr>
<tr>
<td>(mIU/Lt)</td>
<td>(p = 0.468)</td>
<td>(p = 0.577)</td>
<td>(p = 0.082)²</td>
<td>(p = 0.811)</td>
</tr>
<tr>
<td>Final</td>
<td>0.401 [−0.353, 1.154]</td>
<td>0.392 [−0.543, 1.328]</td>
<td>Quadratic: 75.967 [−10.130, 162.065]</td>
<td>0.224 [−0.818, 1.265]</td>
</tr>
<tr>
<td></td>
<td>(p = 0.290)</td>
<td>(p = 0.403)</td>
<td>(p = 0.082)²</td>
<td>(p = 0.67)</td>
</tr>
</tbody>
</table>

Coefficients ([95% C.I.], (p-value)) per hormone unit reported. Asterisks (*) imply statistical significance (p-value<0.100). Ordinary least squares (OLS) estimations were calculated for Mean Blues and EPDS (first, sixth week); robust clustered estimations were calculated for Blues (days 1 through 4), clustering for each patient (due to repeated measuring of Postpartum Blues during the first postpartum days).

Quadratic terms are included in the regression model due to statistical significance; a negative linear coefficient and a positive quadratic coefficient ideally correspond to a U-shaped curve of dependency of psychometric scores on reported hormonal factor (decrease of psychometric score as hormone level starts to increase, for lower hormone levels, and increase of psychometric score as hormone level increases even more, for higher hormone levels).

Indicated statistical significance (at the level of p<0.100) of pregnancy duration (in weeks); pregnancy duration was however included in all multiple regression models as a confounder.

The thyroid gland, thus, is forced to produce greater amounts of hormones, in order to maintain normal free hormone levels in peripheral blood. Although serum total thyroxine concentration rises to the upper normal end, free thyroxine concentration is low during pregnancy and may remain low in the first postpartum weeks (Glinoer, 1997; Hendrick et al., 1998). Varying sensitivity to lower thyroid hormone levels within the euthyroid range antepartum might be implicated for destabilization of mood postpartum.

Other theories regarding the effect of thyroid function on the development of postpartum depression suggest that postpartum mood disorders might be caused by a central nervous system effect of circulating cytokines, which increase in parallel with thyroid antibodies (Harris, 1993). Hendrick et al. (1998) proposed that reduced central serotonin activity might be the link between postpartum mood disturbances and thyroid hypofunction.

Our study bears certain limitations. The small sample and the high dispersion of serum measurements may not have provided enough power to investigate fully their association with postpartum mood disorders, while outliers of TSH and thyroid antibodies, forced us to exclude them from a great part of our analysis. In addition, thyroid values at 6 weeks postpartum could not be obtained, because only few women responded, while no data is available beyond this point of time. The high rate of caesarean section is another weakness which is due to the fact that our hospital serves as a tertiary referral center. Caesarean section, however, is regarded as a weak potential risk factor for the development of postpartum depression (Carter et al., 2006; Robertson et al., 2004).

In conclusion, even in this small sample, the results support the presence of an association of thyroid function within the normal range before delivery and postpartum mood state. Further studies are necessary in order to assess the causative nature of these associations. If our findings are confirmed in
larger prospective studies, screening of thyroid function during a routine antenatal visit might prove useful in assessing the risk for postpartum depression.

Role of funding source
Funding for this study was provided by the Special Account for Research Grants by the National and Kapodistrian University of Athens, SARG 70/3/8259. The funding source had no role in the concept, design and conduct of the study; collection, management and interpretation of the data; drafting, review or approval of the manuscript.

Conflict of interest
All authors declare that they have no conflicts of interest.

Acknowledgements
We thank Dr. Demetrios Rizos and Mr. Hasiakos, who kindly provided the data necessary for our analysis, as well as Dr. Lambrinoudaki who assisted with the preparation of the manuscript.

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