



Antenatal thyroid correlates of postpartum depression

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Summary

We previously found significantly higher T3-resin uptake and nearly significantly lower total thyroxine concentrations at 38 weeks of pregnancy in women with higher postpartum depression ratings. This study further examined the relationship between thyroid status during late pregnancy and antenatal and postpartum depression scores. Thyroid measures were obtained at 32–35, 36, and 37 weeks of pregnancy in 31 women with normal range thyroid hormone levels. Subjects rated their mood at these antenatal time points and every other week between postpartum weeks 2 and 24 on the Edinburgh Postnatal Depression Scale and the Beck Depression Inventory. Mean antenatal thyroxine concentrations and free thyroxine indices correlated significantly and negatively with mean depression scores during each of three postpartum time periods (postpartum weeks 2–6, 14–18, 20–24). Women with total and free thyroxine concentrations that were, respectively, $<10.1 \mu\text{g}/\text{dl}$ and $<1.06 \text{ ng}/\text{dl}$ at all three antenatal time points had significantly higher mean depression scores during all postpartum time periods. The fraction of subjects with pregravid major or minor depression history that was in the low antenatal thyroid group was significantly higher than the fraction of subjects with negative history (5/6 vs. 7/25). Women with antenatal total and free thyroxine concentrations in the lower euthyroid range may be at greater risk of developing postpartum depressive symptoms. Study of the relationships with antenatal thyroid status may provide new insights into the pathophysiology of perinatal mood disturbances.

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1. Introduction

Mood disturbances are alarmingly common among pregnant and postpartum women. The combined prevalence of DSM-IV and Research Diagnostic Criteria (RDC) major and minor depression is approximately 14% during pregnancy and during the first 3 months of postpartum (O'Hara and Swain, 1996; Gaynes et al., 2005). Depressive symptoms appear to be significantly more frequent in postpartum compared to matched, non-puerperal women (O'Hara et al., 1990). The large changes in hormone levels that occur in the perinatal period have long been suspected of playing an etiological role. Studies of hormone correlates of postpartum depression have focused predominantly on estrogen, progesterone or cortisol (Hendrick et al., 1998; Bloch et al., 2003; Breese McCoy et al., 2003; Parry et al., 2003). Relatively few studies have examined the relationship of thyroid variables to perinatal mood. This is surprising since thyroid status has many links to depression and it is well known that the hypothalamic–pituitary–thyroid (HPT) axis undergoes considerable change during pregnancy and the postpartum period. Most overtly hypothyroid patients show mental deficits, predominantly depression (Whybrow et al., 1969; Bauer and Whybrow, 2001) and subclinical hypothyroidism is a risk factor for major depressive disorder (Haggerty and Prange, 1995). Investigators have found subtle dysregulation of the HPT axis in a high percentage of otherwise euthyroid major depressed patients, e.g., blunted or exaggerated TSH responses to thyroid hormone-releasing hormone (TRH) and elevated CSF levels of TRH (Kirkegaard et al., 1979; Gold et al., 1981; Loosen and Prange, 1982; Banki et al., 1988; Bunevicius et al., 1996). Pregnancy places considerable strain on the HPT axis (Glinoe, 1997, 1999). Elevated estrogen levels cause an approximately 150% increase in thyroid binding globulin, requiring the thyroid gland to produce much more hormone to occupy the greater binding space and maintain free hormone levels within the normal range. Serum total thyroxine concentrations rise to the upper end of the normal, non-pregnant range or higher in most pregnant women. Free thyroxine concentrations typically decrease somewhat during pregnancy. Thyroxine concentrations decline for approximately 6 weeks postpartum before plateauing at pregravid levels (Pedersen et al., 1993).

In an earlier study (Pedersen et al., 1993), we found that T3-resin uptake (T3U) was significantly higher and total thyroxine concentrations trended toward being significantly lower at 38 weeks of pregnancy in women who had Hamilton Rating Scale for Depression (HRSD) scores of 10 or higher at one or more postpartum time points. Postpartum thyroid measures were not significantly related to postpartum HRSD scores. The current study was designed to examine more closely the relationship between antenatal thyroid indices and postpartum depression. We hypothesized that women who were more depressed postpartum would have lower thyroxine concentrations and greater T3U values during late pregnancy.

2. Methods and materials

This study was approved by the University of North Carolina School of Medicine Committee for the Rights of Human Subjects and conforms to NIH guidelines.

2.1. Subjects

Subjects ($N = 45$) were recruited from the Department of Obstetrics and Gynecology Faculty Obstetric Clinic at the University of North Carolina Hospitals. Pregnant women who were 18–42 years old and did not meet criteria for current DSM-IV mood, psychotic, anxiety, eating or substance use disorders, had no chronic or significant acute medical disorders (including personal history of thyroid disease) or obstetric complications and who were not taking daily medication other than diphenhydramine, non-opiate analgesics or antibiotics qualified for participation in the study. Women who started birth control pills during the postpartum period were kept in the study. However, data from 14 were excluded from analysis because they delivered prematurely ($N = 3$), were delivered by cesarean section or developed other obstetric complications ($N = 4$), failed to complete self-ratings at the required time points ($N = 4$) or dropped out ($N = 3$). Therefore, data from 31 subjects were included in the final analysis.

2.2. Protocol

The design of this study is summarized in Fig. 1. After obtaining approval from their obstetricians, women were approached at about 25 weeks estimated gestational age (EGA, the time period since the beginning of the last menstruation) by the research nurse who obtained informed consent if they were interested in participating in the study. Potential subjects then completed questionnaires about current psychiatric and medical disorders, obstetric complications and medication usage. Women who answered any of these questions in the affirmative were interviewed to obtain additional details. Potential subjects were interviewed initially by the research nurse face-to-face and then over the phone by Dr. Pedersen, a Board-certified psychiatrist. In addition to confirming the absence of current psychiatric illness, Dr. Pedersen obtained history of depressive episodes prior to the current pregnancy. Those women who met inclusion criteria (see above) were each given a notebook that contained a complete set of questionnaires for each of the 15 time points in the study as well as a sufficient supply of stamped, addressed envelopes so

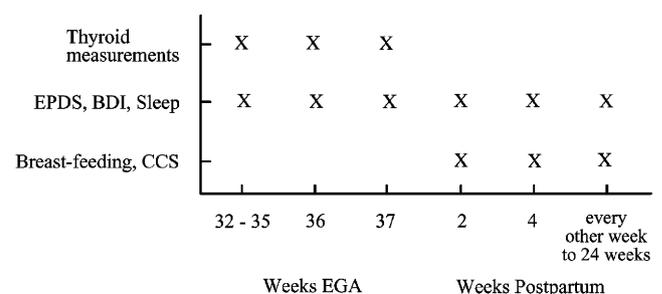


Fig. 1 Schedule of procedures: Thyroid measurements were obtained at 32–35, 36 and 37 weeks estimated gestational age (EGA); Edinburgh Postnatal Depression Scale (EPDS), Beck Depression Inventory (BDI) and sleep self-ratings were obtained at each antenatal and postpartum time point; breast-feeding and childcare stress (CCS) self-ratings were obtained at 2 weeks and every other week out to 24 weeks postpartum.

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