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Review article

Thyroid peroxidase autoantibodies and perinatal depression risk: A systematic review

Manish Dama [a,*], Meir Steiner [b], Ryan Van Lieshout [c]

[a] Life Sciences Program, McMaster University, St. Joseph's Healthcare Hamilton, 100 West 5th Street, Hamilton, ON, Canada L8N 3K7
[b] Departments of Psychiatry & Behavioural Neurosciences and Obstetrics & Gynecology, McMaster University, St. Joseph's Healthcare, 100 West 5th Street, Hamilton, ON, Canada L8N 3K7
[c] Department of Psychiatry & Behavioural Neurosciences, St. Joseph's Healthcare, 100 West 5th Street, Hamilton, ON, Canada L8N 3K7

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ABSTRACT

Background: While thyroid autoantibodies have been linked to depression in general population samples, it is unclear if the immunological milieu of pregnancy alters this association. As a result, we systematically reviewed the literature to determine if abnormal levels of autoantibodies that target thyroperoxidase (TPO-AB) during the perinatal period are associated with an increased risk of antenatal and postnatal depression.

Methods: MEDLINE, EMBASE, PsycINFO, and CINAHL databases were searched through February 2016. Primary studies that examined TPO-AB titers during pregnancy or the postpartum period, and antenatal or postnatal depression were eligible. The quality of each study was assessed using the Newcastle-Ottawa Scale.

Results: Among the eleven articles selected for synthesis, three of these examined associations between TPO-AB and depression both during pregnancy and in the postpartum period. Three of five studies reported statistically significant associations between elevated TPO-AB titers (TPO-AB+) and concurrent depression at 12–25 weeks gestation. Four of five studies found significant associations between TPO-AB+ status at 12–25 weeks gestation and depression in the postpartum period. Two of four studies found links between postpartum TPO-AB and depression concurrently in the puerperium.

Limitations: Lack of adjustment for confounding variables limits causal inference and conclusions about the predictive power of TPO-AB.

Conclusions: Studies suggest that TPO-AB+ in early to mid-pregnancy is associated with concurrent depression and may be predictive of depression in the postpartum period. Future studies with improved methodology are required to better understand the full pathophysiological implications and predictive utility of TPO-AB in perinatal depression.

Contents

* Corresponding author.
E-mail address: damam@mcmaster.ca (M. Dama).

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1. Introduction

Depression during the perinatal period is associated with an increased risk of adverse outcomes for both women and their children. Depression during pregnancy (i.e., antenatal depression) has been linked to elevated rates of obstetrical complications (Grote et al., 2010), as well as depression in the postpartum period (O'hara and Swain, 1996). Postnatal depression is associated with impaired mother-infant bonding (Moehler et al., 2006; O'Higgins et al., 2013) and increased levels of emotional and cognitive problems in offspring during both childhood (Beck, 1998) and adolescence (Hay et al., 2008; Korhonen et al., 2014; Murray et al., 2010; Verbeek et al., 2012).

Research suggests that the etiology of perinatal depression involves a combination of social (Beck, 2001; Lancaster et al., 2010), psychological (Bunevicius et al., 2009a; Leigh and Milgrom, 2008; O'hara and Swain, 1996; Zeng et al., 2015), and biological factors (Leung and Kaplan, 2009; Meltzer-Brody, 2011; Serati et al., 2016; Skalkidou et al., 2012). Indeed, dysregulation of various endocrine systems have been implicated in the pathophysiology of both antenatal and postnatal depression (Meltzer-Brody, 2011; Serati et al., 2016; Skalkidou et al., 2012). Multiple studies examining associations between thyroid hormones (e.g., thyroxine, thyrotropin, and triiodothyronine) and depression during the perinatal period have been suggestive of a link (Abou-Saleh et al., 1998; Ijuin et al., 1998; Lambrinoudaki et al., 2010; Pedersen et al., 2007, 2016, 2012; Sylvén et al., 2013), though a consensus does not exist as to whether clinical syndromes of thyroid dysfunction (e.g., hyper- and/or hypothyroidism) are linked to depression in the perinatal period (Basraon and Costantine, 2011; Lazarus, 1997; Lucas et al., 2001; Pop et al., 1991; Walfish et al., 1992).

During pregnancy, the maternal immune system undergoes many changes to accommodate for the development of the fetus (Zenclussen, 2013) and attempts to return to its pre-pregnancy state in the postpartum period. These changes include alterations in the production of autoantibodies that target thyroid antigens such as thyroid peroxidase (TPO-AB)[1] (Glinoer et al., 1994; Stagnaro-Green et al., 1992). TPO-AB, previously referred to as microsomal antibody (Portmann et al., 1985; Ruf et al., 1987), is the most common type of thyroid autoantibody found in euthyroid individuals (Hollowell et al., 2002) and is associated with various forms of thyroid dysfunction (Hollowell et al., 2002; Vanderpump et al., 1995). Though not yet fully substantiated, multiple studies have suggested that an association may exist between thyroid autoantibodies and depression in general population samples (Carta et al., 2004; Degner et al., 2015; Pop et al., 1998; van de Ven et al., 2012). However, it is not yet clear if similar associations exist for women in the perinatal period (e.g., McCoy et al., 2008; Harris et al., 1989).

Since an understanding of the links between TPO-AB and depression in the perinatal period not only has important pathophysiological implications, but may also have significant clinical utility, we set out to systematically review studies examining associations between abnormal TPO-AB titers in the perinatal period and depression during pregnancy and the puerperium.

2. Methods

2.1. Search strategies for systematic review

We searched MEDLINE, EMBASE, PsycINFO, and CINAHL from their respective inceptions through February 13th, 2016 for studies that examined associations between thyroid indices during pregnancy or the first year of postpartum and antenatal or postnatal depression. The search strategy employed for MEDLINE utilized the following terms: (exp depressive disorder/ or exp depression, postpartum/ or exp depressive disorder, major/ or exp depression/ or exp puerperal disorders/) and (exp obstetrics/ or exp parturition/ or exp mothers/ or exp postnatal care/ or exp prenatal care/ or exp postpartum period/ or exp pregnancy complications/ or exp pregnancy outcome/ or exp prenatal diagnosis/ or exp pregnancy, high-risk/ or exp pregnancy/ or exp perinatal care/ or preconcept*.mp. or peripart*.mp. or antepart*.mp. or postpart*.mp. or antenatal.mp. or postnatal.mp. or maternal nursing.mp. or pregnant.mp.) and (exp hyperthyroidism/ or exp thyroid diseases/ or exp thyrotoxicosis/ or exp goiter/ or exp thyroid function tests/ or exp hyperthyroxinemia/ or exp thyrotropin/ or exp triiodothyronine/ or exp thyroglobulin/ or exp thyroid hormones/ or exp graves disease/ or exp euthyroid sick syndromes/ or exp thyroid dysgenesis/ or exp thyroid hormone resistance syndrome/ or exp congenital hypothyroidism/ or exp thyroid nodule/ or exp hashimoto disease/ or exp postpartum thyroiditis/ or exp thyroid gland/ or exp thyroxine-binding globulin/ or exp hypothyroidism/ or exp thyroid crisis/ or exp goiter, endemic/ or exp goiter, nodular/ or exp hyperthyroxinemia, familial dysalbuminemic/ or exp thyroiditis/ or exp thyroiditis, autoimmune/ or exp thyroiditis, subacute/ or exp thyroiditis, suppurative/ or exp immunoglobulins, thyroid-stimulating/ or exp thyroxine/ or exp triiodothyronine, reverse/or exp thyrotropin-releasing hormone/ or thyroid peroxidase.mp. or subclinical hypothyro*.mp. or subclinical hyperthyro* subclinical dysthyro*.mp. or overt hyperthyro* or overt hypothyro*.mp. or thyroid axis.mp. or thyroid autoantibodies.mp. or autoimmune thyroid disease.mp. or thyroid stimulating hormone receptor*.mp. or thyroidectom*.mp. or thyroid microsomal antibod*.mp. or Ft4.mp. or Ft3.mp. or TG.mp. or TPO.mp. or TRH.mp. or TBG.mp. or t4.mp. or t3.mp. or TSH.mp.) and exp humans/ [mp=title, abstract, original title, name of substance word, subject

[1] *Abbreviations:* TPO-AB, thyroperoxidase autoantibodies; MS-AB, microsomal antibodies; TPO-AB+, high titers of thyroperoxidase autoantibodies; TPO-AB(−), normal titers of thyroperoxidase autoantibodies; HAM-D, Hamilton Rating Scale for Depression; MADRS, Montgomery-Asberg Depression Rating Scale; EPDS, Edinburgh Postnatal Depression Scale; HADS, Hospital and Anxiety Depression Scale; GHQ-30, General Health Questionnaire; POMS-D, Profile of Mood States subscale for symptoms of Depression-Dejection; RDC, Research Diagnostic Criteria; CIDI, Composite International Diagnostic Criteria; DIGS, Diagnostic Criteria for Genetic Studies; and SCID-NP, Structured Interview for DSM-III-R; NOS, Newcastle-Ottawa Scale.