



Review article

Risk factors of new onset anxiety and anxiety exacerbation in the perinatal period: A systematic review and meta-analysis

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ABSTRACT

Background: Even though more than 20% of women meet diagnostic criteria for an anxiety disorder during the perinatal period, very little is known about the predictors of these problems. As a result, we systematically reviewed the literature on risk factors for new onset anxiety and maternal anxiety exacerbation in the perinatal period.

Methods: PubMed, MEDLINE, PsycINFO, CINAHL, Ovid, ProQuest Portal, and Web of Science were searched for studies assessing risk factors for the development of new onset anxiety or anxiety worsening in women during pregnancy and the postpartum period.

Results: 11,759 citations were identified, with 11 studies meeting eligibility criteria. New onset anxiety was assessed in 7 studies, anxiety worsening in 3, and 1 assessed both. Lower educational attainment, living with extended family members, multiparity, a family history of psychiatric disorders, hyperemesis gravidarum, comorbid sleep disorders, and prenatal oxytocin exposure were risk factors for new onset perinatal anxiety, while presence of comorbid psychiatric disorders and prenatal oxytocin were risk factors for anxiety worsening.

Limitations: Studies not explicitly stating whether participants had pre-existing anxiety disorders were excluded. As a result, meta-analysis was not possible for several risk factors.

Conclusions: Risk factors for new onset anxiety and anxiety worsening during the perinatal period include psychological, social, and biological exposures. Given the lack of studies differentiating women with and without pre-existing anxiety disorders, additional research is required in order to determine whether these factors differ from the non-puerperal population, as well as from each other.

1. Introduction

Anxiety disorders are among the most common mental disorders, with global prevalence rates as high as 25% (Remes et al., 2016). Women are twice as likely as men to develop an anxiety disorder in their lifetime, and as many as 20% of women are estimated to experience an anxiety disorder during the first 12 months postpartum (Goodman et al., 2016). For some women, this will be occurring for the first time in their life (i.e., new onset), while others will experience a worsening of existing symptoms or disorders (Ross and McLean, 2006). Unfortunately, fewer than 15% of women with perinatal mental disorders receive treatment for these problems (Smith et al., 2009). This may be due, in part, to the limited attention that has been paid to

perinatal anxiety problems, a relative lack of validated screening measures, and a less than ideal awareness among clinicians of the risk factors for these disorders.

Anxiety disorders are often comorbid with depression, and so the distinction between disorders and their symptoms can sometimes be subtle. Unfortunately, this can lead to missed or inaccurate diagnoses, as well as sub-optimal treatment. As perinatal anxiety is still considered a relatively new area of scientific study research, its financial costs have yet to be estimated. However, postpartum depression is estimated to cost the United States \$5.7 billion annually if left untreated (Diaz and Chase, 2010). As perinatal anxiety prevalence rates are equivalent, if not greater than postpartum depression (Dennis et al., 2016, 2017; Remes et al., 2016), the human and financial burden is potentially

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comparable.

Women with perinatal anxiety can experience significant suffering, with adverse effects for their infant, partner, and other children. These women are at increased risk of obstetric complications, including a difficult labour, pre-eclampsia, and preterm delivery (Dole et al., 2003; Kramer et al., 2009; Kurki et al., 2000; Littleton et al., 2007). Physical symptoms such as nausea and vomiting, heartburn, and muscle aches during pregnancy, as well as increased rates of sick leave from work are also more common in women with perinatal anxiety (Anniverno et al., 2013). Perinatal anxiety may also put the mother-infant bond at risk, as these women are more likely to report decreased perceived bonding with their child (Tietz et al., 2014). These infants are also at increased risk of experiencing cognitive and motor performance deficits (Davis & Sandman, 2010), more difficult temperament, and elevated levels of negative affect (Blair et al., 2011; Brand and Brennan, 2009; Britton, 2011). These adverse effects can extend into childhood, leading to deficits in executive functioning, as well as heightened levels of anxiety in offspring (Bernstein et al., 2005; Buss et al., 2011; Davis and Sandman, 2012).

Despite its high prevalence, perinatal anxiety has received relatively little attention (Farr et al., 2014). Although a number of socio-demographic and psychological risk factors have been identified in the literature, these studies are small in number and their findings are inconsistent. For example, while some studies suggest that younger maternal age and nulliparity are predictors of increased risk, others suggest that older women and those who are multiparous are more likely to experience anxiety in the perinatal period (Bayrampour et al., 2012; Biaggi et al., 2016; Lederman and Weis, 2009; Tearne et al., 2016). Other studies suggest that women with less educational attainment, those who have lower income levels (Biaggi et al., 2016; Yelland et al., 2010), and mothers who receive less social support (Dunkel Schetter, 2011; Peter et al., 2017) are at increased risk.

In terms of psychological risk factors, a past history of mood and/or anxiety disorders are among the most potent predictors of perinatal anxiety development (Faisal-Cury et al., 2009; Martini et al., 2015; Rubertsson et al., 2014). Similarly, women who have experienced abuse in their childhood are at increased risk of experiencing antenatal anxiety (Leeners et al., 2006). Others have highlighted associations between dysfunctional perfectionism (e.g., doubts, parental expectations, concern over mistakes) and postpartum anxiety (Oddo-Sommerfeld et al., 2016). Finally, poor subjective maternal sleep during pregnancy has been linked to heightened levels of postpartum anxiety (Skouteris et al., 2009; Swanson et al., 2010), though some studies have not found an association (Lawson et al., 2015; Tham et al., 2016).

The biological risk factors of perinatal anxiety have yet to be elucidated, despite increasing interest in these as predictors and prognostic factors for anxiety in general population samples. These may be of particular relevance to the perinatal period since during the early stages of pregnancy, from implantation to the second trimester, levels of proinflammatory T-helper cells and their interleukins increase (e.g., interleukin-6, tumor necrosis factor-alpha) (Mor et al., 2011). These have the ability to stimulate the hypothalamic pituitary adrenal (HPA) axis and increase circulating cortisol (Mastorakos and Ilias, 2000; Silverman et al., 2005), which is associated with increased anxiety in both non-puerperal and puerperal populations (Kane et al., 2014; Lenze et al., 2011; Tafet et al., 2005). Following the delivery of a child, the HPA axis remains hyperactive (Duthie and Reynolds, 2013), and HPA hyperactivity has been widely associated with the neurobiology of non-puerperal anxiety and depression (Copeland et al., 2012; Khandaker et al., 2016; Lenze et al., 2011; Tafet et al., 2005; Vogelzangs et al., 2013). Given the intense hormonal changes that occur to women during pregnancy, particularly to the HPA axis (Duthie and Reynolds, 2013), this is an area worthy of further investigation.

Previous systematic reviews of perinatal anxiety (Biaggi et al., 2016; Goodman et al., 2014a, 2016; Ross and McLean, 2006) have focused mainly on estimating the prevalence of anxiety disorders occurring

during the perinatal period. Unfortunately, they have not differentiated women who developed new onset anxiety problems and those who experienced an exacerbation of a pre-existing anxiety disorder, including the social, psychological, and biological predictors of these problems. The literature has shown some differences between risk factors in women with and without pre-existing anxiety disorders, suggesting potential differences in etiology. For example, having a difficult delivery places women without a history of anxiety disorders at risk for postpartum anxiety, whereas no effect has been found in women with pre-existing anxiety (House et al., 2016; Srkalović et al., 2017). Similarly, education status (specifically lower education level) has been shown to be a predictor of new onset perinatal anxiety, whereas this association has not been found in women with pre-existing anxiety (Qiao et al., 2009; Uguz et al., 2007). To our knowledge, no systematic review has attempted to identify and delineate the predictors of new onset anxiety and anxiety worsening as separate clinical presentations. Understanding the predictors of perinatal anxiety in these two groups could assist in the timely and accurate detection of symptoms in women before they develop clinical anxiety or a worsening of their pre-existing symptoms. Perhaps most importantly, such knowledge can inform predictive and preventive strategies for this population at risk. For the purposes of this review, the perinatal period is defined as any time from pregnancy to 12 months postpartum. This is the traditional use of the term and the literature has shown that the prevalence of anxiety disorders is highest during this time (Goodman et al., 2016).

As the risk factors associated with the development and exacerbation of perinatal anxiety are not yet well understood, the aim of this systematic review was to identify predictors of both new onset anxiety and anxiety worsening occurring from pregnancy to 12 months postpartum, and to determine if they differ between these two groups. As the predictors of new onset perinatal anxiety and perinatal anxiety worsening in this systematic review will not be limited to a single domain (i.e., sociodemographic characteristics only), the primary outcome of this review was therefore any factor in any domain shown to be predictive of new onset anxiety or anxiety worsening.

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines and Checklist and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) Guidelines were followed for the current systematic review, which was registered on PROSPERO on March 15, 2017, under the registration number CRD42017057425 (Furtado et al., 2017).

2.1. Data sources and study selection

A literature search of PubMed, MEDLINE, PsycINFO, CINAHL, Ovid Portal, ProQuest Portal, and the Web of Science Portal was conducted from their respective inception through September 18, 2017. A health sciences research librarian was consulted during the creation of the search strategy, which included the use of subject headings as well as keywords, where appropriate. The following combinations of subject headings and keywords found in either the titles or abstracts of articles were used: *anxi** OR *pregnan** OR *perinatal* OR *postpartum* OR *postnatal* OR *generalized anxiety* OR *obsessive compulsive* OR *panic* OR *agoraphobia* OR *post-traumatic stress* OR *stress disorders* OR *social anxiety disorder* OR *social phobia* OR *phobia* OR *anxiety disorder**. Search strategies were adjusted accordingly, based on the database being used. The specific search strategies used in this review are available from the first author upon request. Additionally, an ancestry search, in which reference lists of eligible papers are hand searched, was conducted in order to ensure that all relevant articles had been identified. The search limits for the current review were the English language and human studies.

In this review, only those studies that clearly indicated (in the

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