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Stormy clouds in seventh heaven

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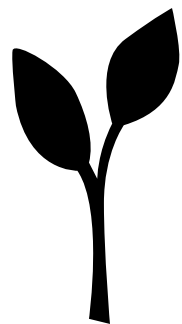
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introduction



chapter 1

About anxiety and depression

Women are at increased risk for the experience of symptoms of anxiety or depression during their reproductive years¹. Incidence rates are highest amongst women between 18 and 45 years of age²⁻⁶. During and outside pregnancy alike, approximately 10-15% of all women experience symptoms of anxiety or depression⁷⁻¹⁰. It has been estimated that in 2030, depression will be in the top 10 of most prevalent diseases¹¹.

In general, symptoms of anxiety and depression may include negative thoughts, loss of energy, sleep disturbances, loss of interest or pleasure, and in some cases suicidal ideations and plans¹². Antenatal (i.e. during pregnancy) or postpartum (i.e. postpartum after delivery) anxiety and depression usually manifest with these same symptoms¹². Box 1 contains the Postpartum Onset specifier for Depressive Disorders, according to the DSM-IV. Risk factors for antenatal symptoms are not necessarily related to pregnancy, though it is known that women who suffered previous pregnancy or infant loss often experience anxiety during the subsequent pregnancy^{13,14}.

Consequences of anxiety or depression during pregnancy or in the postpartum period

Symptoms of anxiety and depression during pregnancy have been associated with several adverse outcomes for mother and child. For example, women tend to seek less prenatal care, continue their use of alcohol and tobacco, and they are at increased risk for postpartum anxiety and depression¹⁵⁻¹⁸. Additionally, low birth weight, preterm delivery, insecure mother-child attachment and emotional and behavioral problems in the child have been found^{19,20}. One of the hypotheses on the mechanism behind this latter observation is that cortisol levels are increased as a result of maternal stress, which influences the development of the fetal brain as cortisol passes the placenta.

BOX 1 SPECIFIER WITH POSTPARTUM ONSET – DSM-IV

“The specifier With Postpartum Onset can be applied to the current (or, if the full criteria are not currently met for a Major Depressive, Manic, or Mixed Episode, to the most recent) Major Depressive, Manic, or Mixed Episode of Major Depressive Disorder, Bipolar I Disorder, or Bipolar II Disorder or to Brief Psychotic Disorder (p.329) if onset is within 4 weeks after childbirth. The symptoms of the postpartum-onset Major Depressive, Manic, or Mixed Episode do not differ from the symptoms in nonpostpartum mood episodes. Symptoms that are common in postpartum-onset episodes, though not specific to postpartum onset, include fluctuations in mood, mood lability, and preoccupation with infant well-being, the intensity of which may range from overconcern to frank delusions. The presence of severe ruminations or delusional thoughts about the infant is associated with a significantly increased risk of harm to the infant.

Postpartum-onset mood episodes can present either with or without psychotic features. Infanticide is most often associated with postpartum psychotic episodes that are characterized by command hallucinations to kill the infant or delusions that the infant is possessed, but it can also occur in severe postpartum mood episodes without such specific delusions or hallucinations. Postpartum mood (Major Depressive, Manic, or Mixed) episodes with psychotic features appear to occur in from 1 in 500 to 1 in 1,000 deliveries and may be more common in primiparous women. The risk of postpartum episodes with psychotic features is particularly increased for women with prior postpartum mood episodes but is also elevated for those with a prior history of a Mood Disorder (especially Bipolar I Disorder). Once a woman has had a postpartum episode with psychotic features, the risk of recurrence with each subsequent delivery is between 30% and 50%. There is also some evidence of increased risk of postpartum psychotic mood episodes among women without a history of Mood Disorders with a family history of Bipolar Disorders. Postpartum episodes must be differentiated from delirium occurring in the postpartum period, which is distinguished by a decreased level of awareness or attention.

Women with postpartum Major Depressive Episodes often have severe anxiety and even Panic Attacks. Maternal attitudes toward the infant are highly variable but can include disinterest, fearfulness of being alone with the infant, or overintrusiveness that inhibits adequate infant rest. It is important to distinguish postpartum mood episodes from the “baby blues”, which affect up to 70% of women during the 10 days postpartum, are transient, and do not impair functioning. Prospective studies have demonstrated that mood and anxiety symptoms during pregnancy, as well as the “baby blues”, increase the risk for a postpartum Major Depressive Episode. A past personal history of nonpostpartum Mood Disorder and a family history of Mood Disorders also increase the risk for the development of a postpartum Mood Disorder. The risk factors, recurrence rates, and symptoms of postpartum-onset Mood Episodes are similar to those of nonpostpartum Mood Episodes. However, the postpartum period is unique with respect to the degree of neuroendocrine alterations and psychosocial adjustments, the potential impact of breast-feeding on treatment planning, and the long-term implications of a history of postpartum Mood Disorder on subsequent family planning.”

Risk factors associated with anxiety or depression during pregnancy or in the postpartum period

Well known risk factors for the onset and persistence of anxiety and depression outside pregnancy are the experience of these symptoms earlier in life, a family history of mental health problems, the experience of traumatic events during childhood, recent major life events, low social support, and specific personality traits such as high neuroticism and low extraversion²¹⁻²⁶. Additionally, personality traits and childhood trauma have been found to moderate the associations between life events and psychopathology^{21,26,27}.

These risk factors also hold for antenatal and postpartum anxiety and depression^{28,28}. Additionally, a few large population-based cohort studies (n>5,000) found that experiencing obstetric events during pregnancy or events that were related to the condition of the newborn (i.e. low birth weight, preterm delivery, congenital malformations, admission to the hospital) increased the risk of symptoms of depression in the postpartum period^{29,30}. In total however, the growing body of literature on the associations between events related to the pregnancy, delivery or newborn and postpartum symptoms of anxiety and depression is inconclusive³¹⁻³⁷.

Screening guidelines

International guidelines recommend screening for perinatal anxiety and depression during the first contact between the woman and the midwife or gynaecologist, and as early postpartum as possible^{38,39}. The American College of Obstetricians and Gynecologists (ACOG) states that women should at least once during the perinatal period be screened, although definitive evidence of benefit is absent. Additionally, they advise to monitor women with current symptomatology or with risk factors for symptomatology closely. The National Institute for Health and Clinical Excellence (NICE) guidelines recommends the use of two questions based on the key symptoms of depression, i.e. low mood and anhedonia, and to ask for specific events in the past period. They recently added the recommendation to use a similar screening tool for anxiety, and a recommendation for further questionnaires or referral to the general practitioner or a psychiatrist in case the first two questions were answered positively. As antenatal anxiety or depression might develop into a clinical disorder when untreated^{28,40}, this seems a valuable addition.

Dutch guidelines for midwives (Koninklijke Nederlandse Organisatie van Verloskundigen, KNOV) include a specific supplement on depression, since 2008⁴¹. They do not recommend

specific screening for current symptomatology, but to ask questions about personal and family history of mental disorders during the first consult, and to be continuously alert on symptoms of depression.

Treatment options

The Dutch multidisciplinary guideline for mental healthcare⁴² recommends to take hormonal changes into account when treating depression, and to educate women on the (continuation of) pharmacological treatment during pregnancy. The NICE has developed a specific multidisciplinary guideline for treatment of pregnant women with symptoms of depression³⁸, in which pharmacological treatment, non-pharmacological treatment or a combination of both is recommended. During pregnancy and the breastfeeding period, women generally prefer non-pharmacological treatment⁴³, as consequences of maternal antidepressant medication use for treating anxiety or depressive disorders are still unclear for the unborn child⁴⁴. Several psychological therapies are used for treating anxiety and depression, such as interpersonal therapy, psychoanalysis, EMDR and cognitive behavioral therapy (CBT). The latter is known to be a widely used and the most studied effective therapy in treating anxiety and depression^{45,46}.

Overall aims of this thesis

The general objective of the current thesis was to unravel part of the etiology of developing symptoms of depression and anxiety in the antenatal period, and the transition of anxiety and depression from the antenatal into the postpartum period. This was accomplished by taking associations with specific life events into account, in order to better understand the development of these symptoms, and to provide evidence for future guidelines on screening.

This thesis focuses on risk factors and screening options in order to be able to prevent symptoms of anxiety or depression and disorders in the future. The prospective, population-based Pregnancy, Anxiety and Depression (PAD) cohort study has been designed to answer these questions amongst others. The final chapter before the general discussion presents the design of a trial including a psychological intervention in pregnant and postpartum women, the Pregnancy Outcomes after a Maternity Intervention for Stressful EmotionS (PROMISES) study.

About the PAD and PROMISES study

The PAD study and the PROMISES study started in 2009. We cooperated with over 100 primary obstetric care centers and seven hospitals in the Netherlands to invite women in their first trimester to participate in the PAD study. In total 7,275 pregnant women were screened for symptoms of anxiety and depression. We sent follow-up questionnaires during the second and the third trimester and at six weeks, three months and six months postpartum. We gathered midwives reports for information about the pregnancy and delivery.

Women who scored above certain cut-off points for anxiety or depression at baseline in the PAD study were invited to participate in the PROMISES study. This is a randomized controlled trial, with which we wanted to gain insight in the mechanism behind the apparent associations found in women with elevated levels of anxiety or depression during pregnancy and a less favorable health of their children, e.g. through fetal programming, a concept introduced originally in studies on cardiovascular disease⁴⁷.

These women received follow-up questionnaires at the same measurement waves as in the PAD study, and additionally at 12 and 18 months postpartum. Their children are currently being tested at 18 months on development and behavior. In 2014, the target of including 300 women into the trial was reached.

Overall outline of the thesis

Chapter 2 discusses the associations between change in antenatal anxiety and depression levels with several categories of life events during pregnancy and personality traits. A distinction is made between general life events and pregnancy related events.

Chapter 3 studies change in anxiety and depression level from early pregnancy to half a year postpartum, by assessing the influence of life events during pregnancy. A distinction is made between general life events and pregnancy related events, similar to chapter 2. Additionally, the difference of these associations between women with and without prevalent antenatal symptoms is assessed, and exploratory analyses with events during delivery or related to the newborn are discussed.

Chapter 4 discusses whether a commonly used tool in identification and screening of antenatal and postpartum anxiety is accurate in predicting individual risk based on antenatal levels.

Chapter 5 demonstrates the predictive accuracy of a tool commonly used in the identification and screening of antenatal and postpartum depression, and explores whether this tool can be optimized by decreasing the number of questions or adding risk factors.

Chapter 6 presents the design of the ongoing randomized controlled trial.

Finally, the results of the analyses and the practical implications are integrated in the general discussion, **chapter 7**. Here, the Wilson and Jungner criteria for screening are applied in order to formulate a recommendation on screening and treatment of antenatal and postpartum anxiety and depression.

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