An Update on Mood and Anxiety Disorders During Pregnancy and the Postpartum Period

Lori L. Altshuler, M.D.; Victoria Hendrick, M.D.; and Lee S. Cohen, M.D.

Because women in the childbearing years are vulnerable to mood and anxiety disorders, physicians in all patient care specialties need to be familiar with the prevalence and course of these disorders, particularly during pregnancy and the postpartum period. Systematic prospective data are limited on the onset of mood and anxiety disorders during pregnancy and the postpartum period as well as on the risk of relapse during these time periods in women with prior histories of the disorders. The literature on mood and anxiety disorders during pregnancy is frequently complicated by the use of various methodologies, procedures, and study populations, and inconsistencies in the postpartum time frame (up to 6 months after delivery) make the literature on epidemiology of postpartum disorders difficult to interpret. This article is an update of available information about the prevalence and course of mood and anxiety disorders in women during pregnancy and the postpartum period.

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Reprint requests to: Lori L. Altshuler, M.D., VA Medical Center, West Los Angeles, B116AA, Bldg. 158, Room 104, 11301 Wilshire Blvd., Los Angeles, CA 90073.

Mood and anxiety disorders in women frequently begin during the childbearing years. Yet, systematic prospective data are limited on the prevalence of mood and anxiety disorders during pregnancy as well as on the risk for relapse in women with prior histories of the disorders. In a recent prospective longitudinal study[1] of 417 pregnant women in England in which depression was measured by the Edinburgh Postnatal Depression Scale, 41 women (9.8%) were depressed during pregnancy and 31 women (7.4%) were depressed at 3 months postpartum. Because women are vulnerable to mood and anxiety disorders, physicians in all patient care specialties need to be familiar with the prevalence and course of these disorders, particularly during pregnancy and the postpartum period.

Many women who have mood and anxiety disorders are treated with psychotropic medications and may be taking such drugs when they conceive. To some extent, any drug or chemical substance administered to the mother is able to cross the placenta unless it is destroyed or altered during metabolism,[2] and the impact of psychotropic medications on the developing fetus is always of concern.[3] However, discontinuing psychotropic medications can lead to relapse,[4–8] and the symptoms common to psychiatric disorders may confer additional risk to the fetus.[9–11] Thus, although the use of psychotropic medications is appropriate in many clinical situations, pharmacologic treatment should include thoughtful weighing by the clinician of the risk of prenatal exposure versus the risk of relapse following drug discontinuation. This article is an update of available information about the prevalence and course of mood and anxiety disorders in women during pregnancy and the postpartum period.

MOOD AND ANXIETY DISORDERS DURING PREGNANCY

Depression

Women in their reproductive years constitute the population at greatest risk for major depression. However, an increase in somatic symptoms has been noted on self-reported depression scales by pregnant women who do not meet the criteria for major depression.[12] Depressive symptoms such as fatigue and changes in sleep and appetite that occur in pregnant women can be difficult to distinguish from the normative experiences of pregnancy. Factors that appear to confer heightened risk for depression during pregnancy include (1) a prior history of depression,[13] (2) young age,[14] (3) limited social support,[15] (4) living alone or having a greater number of children,[16] (5) marital conflict,[17] and (6) ambivalence about the pregnancy.[17]

Literature on the prevalence of depression during pregnancy is frequently complicated by the use of various methodologies, procedures, and study populations. Controlled studies that systematically evaluate the course of depression during pregnancy may arrive at different con-

clusions. In a controlled prospective study,[12] 182 gravid and 179 nongravid women were evaluated prospectively using Research Diagnostic Criteria for major and minor depression, and the rates of depression were equal in gravid and nongravid women. Investigators reported that the highest level of depressive symptomatology occurred at 34 to 38 weeks gestation. Another study that assessed mood state during pregnancy[17] noted that many patients who were depressed in the first trimester frequently experienced improvement in the second and third trimesters. While these 2 studies seem to be at odds, the psychotropic drug status was not mentioned in either study; thus, it is unclear whether the subjects' mood status might have changed as a function of antidepressant treatment or medication discontinuation.

Alterations in antidepressant blood levels may also account for mood changes in pregnant women; observed antidepressant levels reportedly decrease during pregnancy.[18–20] Consequently, women who continue antidepressant treatment throughout pregnancy may have emerging depressive symptoms secondary to a fall in blood antidepressant levels as the pregnancy progresses. The decrease in blood antidepressant levels may be the result of a pregnancy-associated increase in plasma volume occurring by the third trimester or by an increase in hepatic microsomal enzyme-metabolizing activity and renal clearance rates.[18] Blood levels of antidepressants, particularly the tricyclic antidepressants, can be monitored in pregnant women and dose adjustments made as necessary.

The risk for relapse of depressive symptoms is well described for nongravid depressed patients with recurrent mood disorders who discontinue antidepressant medication.[6,14,21,22] Recurrence rates are estimated to be as high as 50% within 6 months following discontinuation of antidepressant treatment. However, little is known about the risk for relapse of depressive symptoms in pregnant women with a prior history of depression who discontinue their antidepressant medication. Depressive relapse during pregnancy is of particular concern because of an increased risk of inadequate prenatal care, poor maternal/fetal nutrition, obstetric complications, and postpartum depression.[13,23–25] Additionally, the potential impact that hypothalamic-pituitary-adrenal dysregulation associated with depression has on fetal well-being is of at least theoretical concern. Decisions regarding medication discontinuation during pregnancy should be made carefully and should take into account the previous psychiatric history and its severity as well as chronicity of the illness as measured by the number of previous episodes of depression.

Manic Depression (Bipolar Disorder)

The impact of pregnancy on the course of manic depressive disorder is unclear; thus, the management of affected women who plan to conceive or are already pregnant poses a significant challenge for clinicians. Some reports document an improvement of manic depressive symptoms in this population.[26,27] On the other hand, data from 186 women and 141 men with manic depression[28] were collected as part of the National Institute of Mental Health Genetics Initiative, a multisite collaborative molecular genetic study. Almost half of the women with manic depression who had been pregnant reported experiencing severe emotional disturbances related to childbearing, and almost one third reported episode onset during pregnancy. The medication status of these women was unavailable.

Discontinuation of mood-stabilizing medications may significantly increase the risk for relapse in nongravid patients with manic depressive illness.[7] However, relapse rates are not well defined in pregnant women with manic depressive disorder who discontinue their mood-stabilizing medications. Recent retrospective data[4,29] indicate that rates of recurrence during the first 40 weeks after lithium discontinuation were similar for gravid and nongravid patients, and there was less risk of relapse with gradual discontinuation of the drug. Other case reports[27] suggest that some manic depressive patients remain emotionally stable during pregnancy despite medication discontinuation.

Panic Disorder

The course of panic disorder during pregnancy is variable. Some women do poorly when attempts are made to discontinue their antipanic medications during pregnancy. Other women experience a diminution of symptoms that allows them to tolerate medication discontinuation. The characteristics that distinguish these patient groups remain to be elucidated. A retrospective study[30] of 20 pregnant patients with active panic symptoms at the time of conception described a marked symptomatic improvement in most of the patients despite the fact that a majority of the women had discontinued their medications at conception. Another retrospective case series[31] of 49 women with pregravid panic disorder noted that 38 patients (78%) were noted to have insignificant change in anxiety status or to have clinical improvement; 10 women (20%) evinced more severe panic symptoms during pregnancy. A more recent prospective study[32] found no diminution in panic symptoms in 9 of 10 women during pregnancy. Finally, a computerized search of the impact of pregnancy and the puerperium on panic disorder[33] identified 8 relevant studies; none were controlled studies, and all but 1 were retrospective. Of the total 215 pregnancies described in the studies, 89 (41%) were associated with improvement of panic symptoms during pregnancy.

Physiologic changes during pregnancy may contribute to the amelioration of panic symptoms in some women. Hormonal changes in pregnancy have been speculated to have anxiolytic affects.[30] Progesterone metabolites possess barbiturate-like activity and may also be anxiolytic.[34]

In addition, pregnancy has been found to decrease sympathetic arousal to a variety of physiologic stimuli; for example, 2 studies reported an attenuation of heart rate and norepinephrine release in response to postural changes in pregnant women.[35,36]

Obsessive-Compulsive Disorder

Few studies have systematically examined the impact of pregnancy and the postpartum period on the course of obsessive-compulsive disorder (OCD), a condition characterized by recurrent intrusive obsessive thoughts and compulsive behaviors. For reasons that are unclear, pregnancy and the puerperium may precipitate or exacerbate OCD. Buttolph and Holland[37] reported that 1 (5%) of 21 men compared with 27 (69%) of 39 women described an onset or worsening of OCD symptoms related to their own or their partner's pregnancy/childbirth. In a retrospective study of 106 women with OCD,[38] 23 (39%) of 59 women who had children experienced the onset or exacerbation of OCD symptoms during pregnancy. Four (80%) of 5 women in the study who had a prior history of abortion or miscarriage also experienced the onset or exacerbation of OCD symptoms during pregnancy. In a retrospective study of the relationship of pregnancy, the puerperium, and premenstruum to the course of OCD,[39] pregnancy was associated with the onset of OCD in 5 (13%) of 38 women. Of 29 women with preexisting OCD who became pregnant, 20 (69%) described no change in symptoms during pregnancy, 5 (17%) described worsening, and 4 (14%) described improvement.

MOOD AND ANXIETY DISORDERS DURING THE POSTPARTUM PERIOD

Depression

The months following childbirth are a time of heightened vulnerability to depressive mood changes. Postpartum depression is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, (DSM-IV)[40(p386)] as a major depressive episode that occurs within 4 weeks of delivery. However, inconsistencies in the postpartum time frame (up to 6 months after delivery) make the literature on the epidemiology of postpartum depression difficult to interpret. Furthermore, reluctance on the part of women to endorse depressive symptoms at a time when they feel pressure to fit the stereotype of happy, fulfilled mothers may lead to reporting bias. Compared with depression occurring at other times in women's lives, postpartum depression is frequently complicated by prominent anxious features.[41] Large and carefully controlled studies in the 6 to 12 weeks after delivery report rates of maternal depression at 12% to 16%.[42–44]

The overlap of depressive symptoms with those of normal childbirth sequelae can confound the clinical identification of postpartum depression. Changes in sleep, appetite, libido, fatigue, and worry are characteristic of both postpartum depression and a normal postpartum period. Risk factors that help to identify postpartum mood disorder include prior episodes of postpartum depression, which is associated with a 50% to 62% risk of subsequent postpartum episode.[45,46] Depressive symptomatology during pregnancy[25,42,47] and family or personal history of major depression[42,43,47] also appear to increase the risk for postpartum depression. Marital discord, stressful life events, and ambivalence about the pregnancy are risk factors not only for depression during pregnancy but also for postpartum depression.[25,42,47–50]

Stressful newborn events, such as health problems and infant irritability, have also been associated with greater risk for postpartum depression.[25,44,51] Two prospective cohorts[52] were analyzed to determine whether women who frequently brought their neonates for (problem-oriented) primary care or emergency department visits were at an elevated risk of having depressive symptoms. Findings revealed that neonatal health care use-patterns predicted maternal risk for postpartum depression; mothers were more likely to have high levels of depressive symptoms if their infants had even 1 emergency department visit. The father's emotional state may also influence the risk for maternal postpartum mood changes. Depression[53] and high levels of expressed emotion in a woman's partner[54] have been associated with greater likelihood of maternal depression in the 6 to 12 months after delivery. Finally, cultural factors may contribute to postpartum mood disturbances. Attention to the new social role as a mother and social structuring of postpartum events plus assistance in the development of mothering skills have been suggested as possible factors that may protect against depressed mood after childbirth.[55]

The etiology of postpartum depression remains unclear. Changes in the reproductive hormonal milieu associated with pregnancy and the postpartum period have been postulated to play a role in mood regulation.[56] It has been hypothesized that the precipitous fall in estrogen concentration after delivery may contribute to the onset of depressive symptoms. Thyroid dysfunction may also contribute to postpartum mood disturbances. In the 6 months after delivery, women experience thyroid dysfunction at a rate of up to 7%[57–59] compared with a rate of 3% to 4%[60] in the general population. In a prospective study[61] of 303 pregnant euthyroid women, 21 (7%) developed postpartum thyroid disorders. Depression was identified in 8 (38%) of the 21 mothers and resolved with treatment of the thyroid dysfunction. Thyroid dysfunction, however, does not appear to account for the majority of cases of postpartum depression. While certain hormones, such as estradiol and corticotropin, merit further exploration, studies have been negative or contradictory for most biological variables thought to be etiologic for postpartum mood disturbance.[56] Data on the extent to which breast-

feeding or weaning may affect mood are similarly inconclusive. Blood sampling in many studies does not control for breast-feeding. Lactation not only influences levels of prolactin, progesterone, estrogen, oxytocin, and cortisol, but also has been associated with both positive and negative mood states.[56]

Prophylactic antidepressant treatment administered immediately after delivery has been noted to dramatically reduce the recurrence of postpartum major depression. A total of 23 pregnant women with histories of at least one previous postpartum episode that fit the DSM-III-R criteria for nonbipolar major depression without psychotic features were evaluated in an open clinical trial.[62] Patients who began antidepressant treatment within 24 hours after delivery relapsed at a rate of 6.7% compared with a rate of 62.5% in women who deferred antidepressant prophylaxis.

Manic Depression (Bipolar Disorder)

The postpartum period is a time of exceptionally high risk for episodes of depression, mania, or psychosis in women with manic depressive illness. The rate of postpartum relapse in women with manic depressive illness varies but has been estimated at 20% to 50%.[63–65] Women with manic depression have a 100-fold greater risk than women with no previous psychiatric history for developing a postpartum psychosis.[66] Although postpartum psychosis can present with features that distinguish it from a typical manic episode (i.e., delirium-like symptoms and confusion),[67] several follow-up studies of women with postpartum psychosis demonstrate recurrence of episodes of manic depression[68,69] or schizoaffective illness,[70] an illness characterized by chronic psychotic symptoms and recurrent manic and depressive episodes.

A few studies have addressed the role of mood-stabilizing medications in preventing a postpartum relapse of manic depressive illness. In a retrospective comparison of recurrence rates and survival functions after lithium discontinuation[4] in 101 women with manic depression, symptoms increased sharply during the postpartum period. Among subjects who remained stable during the first 40 weeks after lithium discontinuation (i.e., during pregnancy), postpartum recurrences (70%) were 2.9 times more frequent than recurrences in non-childbearing women (24%) during weeks 41 through 64. Stewart et al.[71] studied 21 women with a prior history of postpartum psychosis who were treated with lithium either during the third trimester or immediately after delivery of a subsequent pregnancy. Only 2 women (10%) had a recurrence of psychotic illness while on prophylactic lithium. A retrospective study[63] of 27 women with manic depressive disorder found that only 1 (7%) of 14 women taking prophylactic mood-stabilizing agents during the acute puerperium experienced a postpartum relapse compared with 8 (61%) of 13 women who received no antimanic drugs and showed evidence of recurrent affective instability during the 3-month postpartum period. All of these studies underscore the significant morbidity associated with the natural course of manic depressive disorder in new mothers who are not treated prophylactically.

Panic Disorder

The postpartum period appears to be a time of increased vulnerability to recurrent panic symptoms.[31,72,73] In a prospective study of 10 pregnant women with previous histories of panic disorder,[32] 7 (70%) of 10 subjects continued to meet DSM-III-R criteria for panic disorder at all trimester visits. A total of 9 women (90%) with panic disorder—some of whom had experienced a reduction in symptoms during pregnancy—were actively symptomatic in the 1 to 3 months postpartum; the remaining patient who stayed well was also on antipanic medications. Some investigators have hypothesized that the sharp fall in progesterone concentration after delivery may increase vulnerability to panic symptoms.[74] Elevated progesterone during pregnancy produces hyperventilation and a subsequent reduction in P_{CO_2} levels. One theory posits that the rise in P_{CO_2} levels after delivery corresponds with the decline in progesterone and may predispose postpartum women to panic attacks.[30]

The onset of panic disorder during the postpartum period has recently been reported. In the computerized search of 215 pregnancies in 8 relevant studies reported by Hertzberg and Wahlbeck,[33] 83 (38%) of the 215 reviewed pregnancies exhibited onset or exacerbation of panic disorder in the postpartum period. As a consequence of these latest findings, clinicians are urged to differentiate presentations of the more widely known postpartum depression and the newly reported postpartum panic disorder.[75]

Obsessive-Compulsive Disorder

The postpartum period marks a time of increased vulnerability to OCD, even if attempts at medication discontinuation are successful during pregnancy. Buttolph and Holland[37] reported that OCD symptoms in 39 women increased in the postpartum period in 4 women (10%) after the birth of a first child and in 2 women (5%) after the birth of a subsequent child. Another study[76] assessed the occurrence of potentially traumatizing life events among patients with OCD. When examining types of stressful life events, women with OCD were found to be more likely than normal women subjects to report exposure to postpartum events, and high rates of obstetric complications were observed in these patients. Subjects with postpartum OCD also had significantly higher rates of aggressive obsessions to harm their newborn infants. These findings confirm that the postpartum period represents a risk factor for OCD in some individuals and suggest that obstetric complications may be relevant to the development of OCD.[76]

CONCLUSION

Mood and anxiety disorders frequently begin during the childbearing years, and management of women with these disorders poses a substantial challenge to clinicians, especially during pregnancy and the postpartum period. Depressive relapse during pregnancy is of particular concern because of an increased risk of inadequate prenatal care, poor maternal/fetal nutrition, obstetric complications, and postpartum depression. The etiology of postpartum depression remains unclear, but the disorder affects approximately 12% to 16% of new mothers. Recent data suggest that pregnancy is not protective against the risk for relapse after lithium discontinuation in women with bipolar illness. The course of panic disorder during pregnancy and the postpartum period is variable. Some women do poorly when attempts are made to discontinue their medications during pregnancy. Other women experience a diminution of symptoms that allows them to tolerate medication discontinuation. For reasons that are unclear, pregnancy and the puerperium may precipitate or exacerbate symptoms of obsessive-compulsive disorder.

Future prospective studies of women during pregnancy and the postpartum period should begin prior to conception and end several weeks after delivery of the infant. Although the use of psychotropic medications is appropriate in many clinical situations, pharmacologic treatment should include thoughtful weighing by the clinician of the risk of prenatal exposure to psychotropic drugs versus the risk of relapse following drug discontinuation. Decisions regarding medication discontinuation during pregnancy should be made carefully and should take into account the previous psychiatric history and its severity as well as chronicity of the illness as measured by the number of previous episodes of illness.

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