Course of Mood and Anxiety Disorders During Pregnancy and the Postpartum Period

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Because the onset of mood and anxiety disorders often occurs during the childbearing years, many women may be taking psychotropic medications for these disorders when they conceive. These medications easily diffuse across the placenta, and their impact on the fetus is of concern. But discontinuation may lead to relapse, in which case psychiatric symptoms may affect the fetus. Thoughtful treatment planning presents a dilemma to the clinician. Limited data suggest heightened vulnerability to relapse of mood and anxiety disorders in women during the postpartum period. Pregnancy appears to exacerbate symptoms of obsessive-compulsive disorder, while panic disorder patients may remain well after discontinuing medication. Future studies should address the prevalence and relapse rates of mood and anxiety disorders, particularly after medication discontinuation, among pregnant women.
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The onset of mood and anxiety disorders frequently occurs during the childbearing years, and many women with these disorders may be under treatment with psychotropic medications when they conceive. As all psychotropic medications diffuse readily across the placenta, their impact on the developing fetus is of concern. However, medication discontinuation can lead to relapse,[1–3] and psychiatric symptoms may also confer risk to the fetus.[4–6] Clinicians are thus frequently faced with the dilemma of how to advise their patients regarding thoughtful treatment planning.

Pregnancy has been described as a time of emotional well-being during which some psychiatric disorders become quiescent.[7–10] However, few systematic prospective data are available regarding prevalence of mood and anxiety disorders during pregnancy and risk for relapse in women with prior histories of these illnesses who discontinue medications when they become pregnant. This paper addresses available information regarding the prevalence and course of these illnesses during pregnancy and the postpartum period.

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DEPRESSION DURING PREGNANCY

Depressive symptoms in pregnant women, such as fatigue and changes in sleep and appetite, can be difficult to distinguish from normative experiences of pregnancy. Elevated levels of somatic symptoms have been reported on self-report scales of depression by pregnant women who do not meet criteria for major depression.[11,12] Furthermore, the literature on the prevalence of depression during pregnancy is complicated by the various methodologies and procedures used and study populations assessed. In one of the few controlled studies,[12] in which 182 gravid and 179 nongravid women were evaluated prospectively with Research Diagnostic Criteria for major and minor depression, rates of depression were equal in gravid and nongravid women. On the basis of these data, pregnancy did not appear to be protective against depression. Factors that appear to confer heightened risk for depression during pregnancy include (1) prior history of depression,[13] (2) younger age,[14] (3) limited social support, (4) living alone, greater number of children,[15] (5) presence of marital conflict,[10] and (6) ambivalence about the pregnancy.[10]

The course of depression across pregnancy has been systematically evaluated in several studies. For example, one study[10] in which mood was assessed across pregnancy noted that many patients who were depressed in the first trimester frequently experienced improvement in the second and third trimesters. A larger prospective study[12] assessed 182 pregnant women from the second trimester through 9 weeks postpartum. The investigators reported that the highest level of depressive symptomatology occurred at Weeks 34 to 38 of gestation. While these two

studies seem at odds, psychotropic medication status of the patients was not mentioned in either case, and thus it is not clear whether subjects' mood status changed as a function of antidepressant treatment or discontinuation. Little is known about risk for relapse in pregnant women with histories of depression who discontinue their medications. In contrast, risk for relapse is increasingly well described for nongravid depressed patients with recurrent mood disorder who discontinue antidepressant therapy.[1,14,16,17] Recurrence rates for these patients are estimated as high as 50% within 6 months following discontinuation of antidepressant treatment. The implications of these studies for women with recurrent mood disorders who discontinue antidepressant treatment during pregnancy remain unclear. Depressive relapse during pregnancy is of particular concern because of increased risk of inadequate prenatal care, poor nutrition, obstetric complications, and postpartum depression.[13,18–20] In addition, the potential impact of hypothalamic-pituitary adrenal dysregulation associated with depression on fetal well-being is of at least theoretical concern. Thus, decisions regarding medication discontinuation during pregnancy should be made carefully and should take into account previous psychiatric history and its severity as well as the chronicity of illness as measured by the number of previous episodes of depression.

One additional factor that may account for changes in mood across pregnancy in women treated with antidepressant medication may be changes in plasma drug levels across pregnancy. Observed antidepressant levels have been reported to decrease across pregnancy.[21,22] This result may be due to pregnancy-associated increases in plasma volume and hepatic microsomal enzyme activity and/or in renal clearance rates.[23] For women who continue antidepressant treatment during pregnancy, depressive symptoms secondary to a fall in serum antidepressant levels may emerge as the pregnancy progresses.[21] Serum levels of antidepressants (particularly of tricyclics) can be monitored in pregnant women, however, and dose adjustments made as necessary.

DEPRESSION DURING THE POSTPARTUM PERIOD

Postpartum depression is defined in the DSM-IV as a major depressive episode that occurs within 4 weeks of delivery. Inconsistencies in the time frame used to delineate the postpartum period—ranging from 4 weeks to 6 months after delivery—make the literature on the epidemiology of postpartum depression difficult to interpret. Furthermore, reluctance to endorse depressive symptoms at a time when women may feel pressure to fit the stereotype of happy, fulfilled mothers may lead to a reporting bias. The largest and most carefully controlled studies report rates of depression of 12% to 16% during the 6 to 12 weeks after delivery.[24–26] Risk factors for postpartum mood disorder include prior postpartum depression, which is associated with a 50% to 62% risk of subsequent postpartum episode.[22,27] Depressive symptomatology during pregnancy[20,24,28] and family or personal histories of major depression[10,24–26,28] also appear to increase the risk for postpartum depression. Prophylactic antidepressant treatment immediately after delivery has been noted to reduce relapse rates dramatically. In one open study of 23 pregnant women with histories of postpartum depression, with or without past histories of nonpuerpural affective disorder,[29] patients who began antidepressant treatment within 24 hours after delivery relapsed at a rate of 6.7%, compared with a 62% rate noted in women who deferred antidepressant prophylaxis.

Marital discord, stressful life events, and ambivalence about pregnancy are risk factors not only for depression during pregnancy but also for postpartum depression.[10,20,24,26,28,30,31] Stressful newborn-associated events, such as health problems and infant irritability, have also been associated with greater risk for postpartum depression.[20,26,32] The father's emotional state may also influence the risk for postpartum mood changes. Depression[33] and high levels of expressed emotion[34] in a woman's partner have been associated with greater likelihood of maternal depression in the 6 to 12 months after delivery. Cultural factors may also contribute to postpartum mood. For example, attention to the new social role of mother and to the social structuring of postpartum events, as well as assistance in the development of mothering skills, have been suggested as possible factors that may protect against depressed mood after childbirth.[35]

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. 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 disturbance. Rates of postpartum hypothyroidism are relatively high, especially in the first 6 months after delivery, and the rate of thyroiditis in this time period is estimated to be as high as 9%[36] compared with 3% to 4% noted in the general population. Postpartum thyroid abnormalities have been linked with mild depressive symptoms that resolve after normalization of thyroid function.[37–40] Thyroid dysfunction, however, does not appear to account for the majority of cases of postpartum depression. To date, studies of the potential role of other biological factors—including gonadal hormones, prolactin, oxytocin, cortisol, and β-endorphins—have failed to identify a specific etiology for postpartum mood disturbance. Data on the extent to which breastfeeding or weaning may affect mood are similarly inconclusive.[41]

BIPOLAR ILLNESS IN PREGNANCY AND THE POSTPARTUM PERIOD

The impact of pregnancy on the course of bipolar disorder is unclear. While psychosis can occur during pregnancy in bipolar women,[42,43] several reports document an improvement in symptoms in this population.[44–46] In one study,[45] 80% of patients with affective illness (predominantly bipolar) experienced an improvement or a diminution of symptoms of their mood disorder during pregnancy.

Relapse rates in pregnant women with bipolar disorder who discontinue mood-stabilizing medication are not well defined. Case reports suggest that some patients maintain euthymia during pregnancy despite medication discontinuation.[46,47] However, recent research demonstrates that discontinuation of mood stabilizers significantly increases risk for relapse in nongravid bipolar patients.[2,48] Particularly relevant for the pregnant bipolar patient is the apparent increase in the risk for relapse associated with abrupt medication discontinuation.

The rate of postpartum relapse in women who suffer from bipolar illness has been estimated at 33% to 50%.[8,49] Many of these patients present with postpartum psychosis. Although postpartum psychosis can be present with features that distinguish it from a typical manic episode (i.e., delirium-like symptoms and confusion),[50] several follow-up studies of women with postpartum psychosis demonstrate recurrence of episodes of bipolar disorder[51,52] or schizoaffective illness.[53]

As in nonpsychotic postpartum depression, the likelihood of recurrent episodes of puerperal psychosis after an index episode is great, with estimates as high as 75% to 90%. (The initial risk for postpartum psychosis has been estimated at 1 in 1000.[10]) Few studies have addressed the role of mood stabilizers in preventing a postpartum relapse. In one study,[54] 21 women with a history of postpartum psychosis were treated with lithium during a subsequent pregnancy or at the time of delivery. A relapse rate lower than expected was noted in the lithium-treated group. Another prospective study of 22 women with bipolar disorders[55] reported that only 1 of 14 women taking prophylactic agents experienced a postpartum relapse compared with 8 of 13 women not taking antimanic medication. These studies underscore the morbidity associated with the natural course of bipolar disorder in puerperal women who are not prophylactically treated.

PANIC DISORDER IN PREGNANCY AND THE POSTPARTUM PERIOD

Several case reports and studies of pregnant patients with panic disorder suggest a reduction of symptoms during pregnancy in some of these patients.[56,57] For example, a retrospective study 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 medication at conception.[58] Other retrospective studies have similarly found that patients were able to reduce or discontinue medications during a pregnancy without a relapse of their panic disorder. However, the only prospective study[55] found no diminution in panic symptoms during pregnancy. However, many patients required an increase in medication to maintain antipanic status. The course of panic disorder during pregnancy thus may be variable. Subgroups of women may do poorly when attempts at medication discontinuation are made, but others may be able to tolerate medication discontinuation and may experience diminished symptoms. Patient characteristics that distinguish these groups remain to be elucidated.

Physiologic changes occurring in pregnancy may contribute to the amelioration of panic symptoms in some women. Hormonal changes in pregnancy have been speculated to have anxiolytic effects,[58] and progesterone metabolites possess barbiturate-like activity and may also be anxiolytic.[59] In addition, pregnancy has been reported to decrease sympathetic arousal to a variety of physiologic stimuli. For example, two studies have reported an attenuation of heart rate and norepinephrine release in response to postural changes in pregnant women.[60,61]

While the course of panic disorder during pregnancy is unclear, the postpartum period appears to be a time of increased vulnerability to recurrent panic symptoms.[56,62–65] In the only prospective study,[55] 90% of panic disorder patients (some of whom had experienced a reduction in symptoms during pregnancy) were actively symptomatic in the first 1 to 3 months postpartum. The 10% of patients who remained well were taking antipanic medications. Some researchers have hypothesized that the sharp fall in progesterone concentration after delivery may increase vulnerability to panic symptoms.[66] 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.[58]

OBSESSIVE-COMPULSIVE DISORDER IN PREGNANCY AND THE POSTPARTUM PERIOD

Few studies have systematically examined the impact of pregnancy and the postpartum period on the course of obsessive-compulsive disorder (OCD). Buttolph and Holland,[67] in a retrospective evaluation of 39 women and 21 men, found that one man (5%) and 27 women (69%) described onset or worsening of OCD symptoms as related to their own or the partner's pregnancy or childbirth. Another retrospective study[68] of 106 women with OCD found

that, of the 59 women with children, 23 (39%) had symptom onset of OCD during pregnancy. Of 5 women who had abortions, 4 (80%) experienced symptom onset or exacerbation of OCD during pregnancy. In a prospective study of 14 patients who were not taking medications during pregnancy (8 who were not taking medications at the time that they conceived, and 6 who were taking medications until they conceived, then chose to discontinue), 43% required a reinstitution of their medications during pregnancy due to relapse (Sichel DA, oral communication, 1996). The characteristics of the subgroups who relapsed remain to be further evaluated. Of those patients with a history of OCD who were able to remain off medications during pregnancy (N = 8), all had a recurrence or an exacerbation of their symptoms in the postpartum period (Sichel DA, oral communication, 1996). In women with a vulnerability to OCD, pregnancy may precipitate the inception of illness, for unclear reasons. As with panic disorder, the postpartum period marks a time of increased vulnerability to OCD even if attempts at medication discontinuation are successful during pregnancy. Factors that predict the course of OCD during pregnancy remain to be elucidated.

CONCLUSIONS

In summary, the course of mood and anxiety disorders in pregnancy deserves further investigation. Issues to be addressed in future studies include the prevalence and rates of relapse of these disorders in pregnancy, particularly after medication discontinuation. Future studies are needed in which patients are followed prospectively, beginning prior to conception and extending at least several weeks after delivery. Pregnancy does not appear to protect against depression, or to exacerbate its course, in women without pregravid histories of affective disorder. However, subgroups of women with pregravid histories may experience recrudescence or persistence of symptoms in pregnancy. Given the extent to which mood and anxiety disorders cluster in women during childbearing years, future studies aimed at understanding the course of these illnesses during pregnancy in women who elect to discontinue medications at the time of conception will help guide treatment options for patients. Bipolar patients may experience lower rates of relapse during pregnancy compared with other times, but this hypothesis requires further prospective assessment. Data for panic disorder, which are mostly retrospective, suggest that some pregnant patients are able to remain well after medication discontinuation. OCD is the only disorder for which the methodologically limited data show that symptoms may escalate in pregnancy. Although data are limited, the current literature consistently describes the postpartum period as a time of heightened vulnerability to relapse of mood and anxiety disorders.

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