Anxiety Disorders During Pregnancy and the Postpartum Period: A Systematic Review

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Objective: The postpartum period is recognized as a time of vulnerability to affective disorders, particularly postpartum depression. In contrast, the prevalence and clinical presentation of anxiety disorders during pregnancy and the postpartum period have received little research attention. In this article, we review the medical literature as it relates to the prevalence and clinical presentation of panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder during pregnancy and the postpartum period.

Data Sources: MEDLINE (1966 to July 2005 week 1) and PsycInfo (1840 to July 2005 week 1) were searched using combinations of the following search terms: *pregnancy, childbirth, postpartum, panic disorder, phobia, obsessive-compulsive disorder, posttraumatic stress disorder*, and *generalized anxiety disorder*.

Study Selection: All relevant papers published in English and reporting original data related to perinatal anxiety disorders were included.

Data Extraction: Studies were examined for data related to the prevalence, presentation, predictors/risk factors, new onset, course, and treatment of anxiety disorders during pregnancy and the postpartum period.

Data Synthesis: Anxiety disorders are common during the perinatal period, with reported rates of obsessive-compulsive disorder and generalized anxiety disorder being higher in postpartum women than in the general population. The perinatal context of anxiety disorders presents unique issues for detection and management.

Conclusions: Future research is needed to estimate the prevalence of perinatal anxiety disorders more precisely, to identify potential implications of maternal anxiety disorders for maternal quality of life and child development, and to determine safe and effective treatment methods.

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A growing body of research has characterized the clinical presentation, prevalence, and treatment of major depressive disorder during the perinatal period, i.e., during pregnancy and the first year postpartum.[1–3] It is now commonly held that approximately 13% of women will exhibit symptoms of depression during pregnancy and/or the postpartum period.[4,5] Although significant gaps in the research remain, both pharmacotherapy and psychotherapy are effective treatments for perinatal depression.[6–9]

Anxiety disorders in the perinatal period have received less research attention. Recent findings indicate that symptoms of anxiety are common during pregnancy and the postpartum period[10,11] and that maternal symptoms of anxiety during pregnancy are associated with adverse fetal and developmental consequences.[12] Overactivity of the maternal neuroendocrine system has been implicated in negative health outcomes seen in fetuses born to stressed or anxious mothers. Fetal exposure to

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elevated levels of hormones (particularly cortisol) may contribute to premature labor and delivery.[13,14] Maternal exposure to stress and anxiety may precipitate the release of catecholamines that can result in maternal vasoconstriction and ultimately a limitation of oxygen and vital nutrients to the fetus.[15] The exposure of the fetus to maternal stress and increased levels of adrenal hormones therefore has possible consequences for fetal central nervous system development and specifically glucocorticoid brain receptor development.[14,16]

The peak age at onset for anxiety disorders in women occurs in the mid- to late-20s,[17] during the childbearing years. Considering the high prevalence of mood and anxiety disorders in women, it follows that substantial numbers of women will exhibit symptoms and may therefore benefit from treatment for anxiety disorders during pregnancy and the postpartum period. There is consequently a pressing need to broaden the study of perinatal mental health to include rigorous empirical study of perinatal anxiety disorders.[18] This article reviews the published literature as it relates to perinatal panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, and generalized anxiety disorder.

METHOD

Two electronic databases, MEDLINE (1966 to July 2005 week 1) and PsycInfo (1840 to July 2005 week 1), were searched using combinations of the following search terms: *pregnancy, childbirth, postpartum, panic disorder, phobia, obsessive-compulsive disorder, posttraumatic stress disorder*, and *generalized anxiety disorder.* Additional publications were identified from reference lists of retrieved articles. All relevant papers published in English and reporting original data related to perinatal anxiety disorders were included. Due to space restrictions, literature reporting on anxiety symptoms or subsyndromal anxiety and papers reviewing theoretical perspectives on perinatal anxiety disorders were excluded from the review. Only 2 studies could be identified that reported on phobia during the perinatal period,[19,20] and as such perinatal agoraphobia and social phobia were not included in this review. Although large case series have been included, small case series ($N < 5$) and individual case reports have been included only where illustrative.

RESULTS

Panic Disorder

Panic disorder is characterized by sudden, recurrent, and unpredictable panic attacks, associated with persistent worry about the possibility of having future panic attacks.[21] Symptoms of panic attacks typically include shortness of breath, heart palpitations, chest pain, dizziness, and fear of losing control or dying. Approximately 50% of individuals with panic disorder also have comorbid major depression.[21]

Prevalence of perinatal panic disorder. Despite variability in assessment times and procedures, relatively consistent prevalence rates ranging from 1.3% to 2.0% have been reported for panic disorder during the perinatal period (Table 1).[19,20,22–24] In comparison, the DSM-IV reports lifetime prevalence rates of panic disorder ranging from 1.5% to 3.5% and 1-year prevalence rates of 1.0% to 2.0%, with a typical age at onset at late adolescence to the mid-30s.[21]

Presentation and predictors of perinatal panic disorder. Although symptoms of panic during the perinatal period are typical of symptoms in the general population, they are often interpreted in the context of the perinatal state. For example, women may interpret panic attacks during pregnancy as an indication that something is wrong with the fetus.[34] In a qualitative, phenomenological study of 6 postpartum women with panic disorder, women reported feeling unable to leave their homes to take their children to groups and activities and worried about the long-term impact of their panic disorder and the resulting isolation on their children.[35]

Although no literature has reported risk factors for or predictors of perinatal panic disorder, there is some evidence from retrospective studies of a relationship between lactation/weaning and panic symptoms. In a report including 43 breastfed babies, weaning of 12 (28%) was associated with exacerbation of panic in the mother.[36] In another study of 22 women, 1 participant reported onset of panic at weaning.[37] A third study found that 9 of 16 women who did not breast-feed their babies had panic attacks during the postpartum period, as compared to only 2 of 17 women who breast-fed.[38] Six of these women reported onset of panic attacks with weaning. Controlled, prospective studies are needed to determine whether breastfeeding reduces, and/or weaning increases, risk for panic disorder.

New onset of panic disorder. Few studies have examined incidence of perinatal panic disorder (Table 2). A retrospective study of first panic in a sample of 64 childbearing women treated at an academic research clinic found that significantly more women reported onset during the first 12 weeks postpartum than would be expected by chance (10.9% vs. 0.92%).[39] The mean time of onset was 7.3 weeks postpartum (range, 1–12 weeks). However, due to the retrospective nature of this study, it is possible that women associated onset of symptoms with childbirth due to its prominence in the memory as a major life event. Controlled research is needed to determine if the postpartum period is associated with increased risk for new onset of panic disorder.

Course of preexisting panic disorder. Many women experience pregnancy following the onset of panic disorder, and some limited research has described the perinatal

Table 1. Prevalence of Anxiety Disorders During the Perinatal Period

Study	Outcome	Assessment Time	N	Prevalence (%)	Notes
Panic disorder					
Smith et al (2004)[22]	PRIME-MD Brief Patient Health Questionnaire	Any point in pregnancy	387	2.0	
Zar et al (2002)[23]	Anxiety Disorders Interview Schedule-Revised	32 weeks' gestation	453	1.3	386 participants interviewed; 67 assumed negative for anxiety disorders (did not meet prescreen criteria)
Sutter-Dallay et al (2004)[20]	Mini-International Neuropsychiatric Interview	Third trimester of pregnancy	497	1.4	Excluded multiple pregnancies, premature births, and cesarean delivery
Wenzel et al (2001)[24]	Modified nonpatient SCID	Variable weeks postpartum	788	1.5	All participants had at least moderate symptoms of depression
Wenzel et al (2005)[19]	Nonpatient SCID	8 weeks postpartum	147	1.4	
Obsessive-compulsive disorder					
Zar et al (2002)[23]	Anxiety Disorders Interview Schedule-Revised	32 weeks' gestation	453	0.2	386 participants interviewed; 67 assumed negative
Sutter-Dallay et al (2004)[20]	Mini-International Neuropsychiatric Interview	Third trimester of pregnancy	497	1.2	Excluded multiple pregnancies, premature births, and cesarean delivery
Wenzel et al (2005)[19]	Nonpatient SCID	8 weeks postpartum	147	2.7	
Wenzel et al (2001)[24]	Modified nonpatient SCID	Variable weeks postpartum	588	3.9	All participants had at least moderate symptoms of depression
Posttraumatic stress disorder					
Loveland Cook et al (2004)[25]	Diagnostic Interview Schedule	Any point in pregnancy	744	7.7	Economically disadvantaged sample, 23% under 19 years of age
Soderquist et al (2004)[26]	Traumatic Event Scale	32 weeks' gestation	1224	2.3	
Ayers and Pickering (2001)[27]	MMPI-2 PTSD Scale	36 weeks' gestation	222	8.1	
Sutter-Dallay et al (2004)[20]	Mini-International Neuropsychiatric Interview	Third trimester of pregnancy	497	0	Excluded multiple pregnancies, premature births, and cesarean delivery
Soet et al (2003)[28]	Traumatic Event Scale	4 weeks postpartum	103	1.9	Childbirth specified as traumatic event
Creedy et al (2000)[29]	Postpartum Stress Symptoms Interview (via telephone)	4–6 weeks postpartum	400	5.6	Childbirth specified as traumatic event
Czarnocka and Slade (2000)[30]	PTSD-Questionnaire derived for this study from the PTSD Interview	6 weeks postpartum	264	3.0	Childbirth specified as traumatic event
Ayers and Pickering (2001)[27]	PTSD Symptom Scale	6 weeks postpartum	218	6.9	Childbirth specified as traumatic event
Wenzel et al (2005)[19]	Nonpatient SCID	8 weeks postpartum	147	0	Childbirth specified as traumatic event
Ayers and Pickering (2001) [27]	PTSD Symptom Scale	6 months postpartum	201	3.5	Childbirth specified as traumatic event
Wijma et al (1997)[31]	Survey developed for the study	Within 1 year postpartum	1640	1.7	Childbirth specified as traumatic event
Generalized anxiety disorder					
Sutter-Dallay et al (2004)[20]	Mini-International Neuropsychiatric Interview	Third trimester of pregnancy	497	8.5	Excluded multiple pregnancies, premature births, and cesarean delivery
Wenzel et al (2003)[32]	Nonpatient SCID	8 weeks postpartum	68	4.4	Duration criterion shortened to 8 weeks ("since birth of the child")
Wenzel et al (2005)[19]	Nonpatient SCID	8 weeks postpartum	147	8.2	Duration criterion shortened to 8 weeks ("since birth of the child")
Ballard et al (1993)[33]	Psychiatric Assessment Scale (RDC diagnosis)	6 months postpartum	148	6.1	Not all participants were interviewed (identified as probable cases using EPDS)

Abbreviations: EPDS = Edinburgh Postnatal Depression Scale, MMPI = Minnesota Multiphasic Personality Inventory, PRIME-MD = Primary Care Evaluation of Mental Disorders, RDC = Research Diagnostic Criteria, SCID = Structured Clinical Interview for DSM-IV.

Table 2. New Onset of Anxiety Disorders During the Perinatal Period[a]

Study	Design	N	Incidence	Onset
Panic disorder				
Sholomskas et al (1993)[39]	Interviews regarding chronology of panic disorder with childbearing women treated at a tertiary care center	64	10.9% (N = 7)	7.3 weeks postpartum
Villeponteaux et al (1992)[37]	Questionnaire regarding changes in panic symptoms during pregnancy administered to former panic disorder outpatients	22	9.1% (N = 2)	Within 3 months postpartum
Northcott and Stein (1994)[36]	Retrospective questionnaire regarding changes in panic symptoms during pregnancy administered to former panic disorder outpatients	97	3% (N = 3) 9% (N = 9)	During pregnancy Within 6 months postpartum
Obsessive-compulsive disorder				
Maina et al (1999)[40]	Retrospective interviews with consecutive OCD outpatients and healthy comparison sample to establish stressful life events potentially associated with OCD onset	33	25% (N = 8)	During postpartum period
Neziroglu et al (1992)[41]	Questionnaire regarding chronology of OCD relative to childbearing completed by female OCD outpatients	59	39% (N = 23)	During pregnancy
Williams and Koran (1997)[42]	Standardized telephone interview regarding clinical course of OCD during and after pregnancy with OCD outpatients	38	13% (N = 5) 0% (N = 0)	During pregnancy During postpartum period
Buttolph and Holland (1990)[43]	Questionnaire regarding chronology of OCD relative to pregnancy and childbirth sent to OCD outpatients	39	22% (N = 6) 29.5% (N = 8)	During pregnancy During postpartum period (triggered by birth and care of child)
Labad et al (2005)[44]	Retrospective semistructured interview regarding relationship between reproductive cycle events and OCD with female outpatients	46 (17 at least 1 live birth)	6.0% (N = 1) 18.0% (N = 3)	During third trimester of pregnancy Within 1 month postpartum
Posttraumatic stress disorder				
Ayers and Pickering (2001)[27]	Prospective study of women recruited from antenatal clinics between 16–36 weeks' gestation	218	3.2% (N = 7)	6 weeks postpartum

[a]Studies reported in Table 1 assumed that generalized anxiety disorder (GAD) had onset following childbirth, but no studies to date have conducted baseline assessments in order to assess incidence of perinatal GAD.
Abbreviation: OCD = obsessive-compulsive disorder.

course of illness in these women. Although there are conflicting findings, a general pattern of improvement in panic symptoms during pregnancy, followed by worsening during the postpartum period, has been reported in retrospective studies and case reports (Table 3).[36,38,49,50] However, other evidence (see, for example, references 45–48) suggests that the most common effect of perinatal status on panic disorder may be no change in symptom severity. For example, one longitudinal study of 22 women with panic disorder and comorbid mood disorder followed over 5 years found that the most common effect of pregnancy on panic symptoms was no change from baseline during pregnancy (31 pregnancies, 69%).[45] However, when change did occur, it was likely to be a decrease in symptoms (12 pregnancies, 27%). Similarly, most women did not experience a change in symptom intensity during the postpartum period (31 pregnancies, 69%). However, when change did occur, it tended to be an increase in or onset of symptoms (14 pregnancies, 31%), while none of the women reported a decrease in symptoms during the postpartum period. An interesting finding in this report was that the pattern of change (if any) in panic symptoms was not consistent across gestations for the majority of women who experienced more than 1 pregnancy (9 of 14 women, 64%).[45] These results suggest that pregravid symptom severity may be the best predictor of the perinatal course of panic disorder for most women.

Treatment of perinatal panic disorder. Research evidence to guide treatment of perinatal panic disorder is extremely limited, as no controlled or uncontrolled studies have been published. Case reports have described successful treatment with antipanic medications, particularly imipramine,[51,52] and cognitive-behavioral therapy.[53] Other self-care strategies, such as elimination of caffeine, reduction of sleep deprivation, and relaxation techniques, have been recommended if avoidance of pharmacotherapy is desired and possible.[50]

Appropriate differential diagnosis is important before initiating treatment for an anxiety disorder during the perinatal period, although this issue has not been addressed in the research literature. Thyroid dysfunction and anemia are commonly seen in perinatal women and may be associated with symptoms of panic or generalized anxiety. Preeclampsia can also be associated with

Table 3. Course of Anxiety Disorders During the Perinatal Period[a]

Study	N	Inclusion Criteria and Design	Pregnancy[b]			Postpartum[b]			Notes
			Symptom Decrease	No Change	Symptom Increase	Symptom Decrease	No Change	Symptom Increase	
Panic disorder									
Villeponteaux et al (1992)[37]	22 (44 pregnancies)	At least 1 pregnancy after onset of panic disorder, no use of psychotropic medications	66% (29)	18% (8)	16% (7)				5 women (23%) noted return of panic attacks within 3 months postpartum; 1 woman (4.5%) noted return of panic attacks at weaning
Wisner et al (1996)[45]	22 (45 pregnancies)	Panic and comorbid mood disorder diagnosis; followed over 5 years	27% (12)	69% (31)	4.4% (2)	0% (0)	69% (31)	31% (14)	3 women (14%) had psychotropic medication exposure. Pattern of change across perinatal period was inconsistent for 9 of 14 multiparous women
Northcott and Stein (1994)[36]	46 (67 pregnancies)	Retrospective survey of clinic patients with at least 1 pregnancy after onset of panic disorder	43% (29)	24% (16)	33% (22)	18% (12)	19% (13)	63% (42)	Pattern of change across perinatal period was inconsistent for 9 of 20 multiparous women
Cohen et al (1994)[46]	49	Retrospective chart review of women with pregravid panic disorder across pregnancy	20% (10)	57% (28)	20% (10)				65% (N = 32) took antipanic medication at some point during pregnancy. One woman experienced heightened and reduced symptoms of panic at different times during her pregnancy
Cohen et al (1994)[47]	40	Retrospective chart review and interviews with women with pregravid panic disorder to 12 weeks postpartum				7.5% (3)	57.5% (23)	35% (14)	Proportion of participants taking antipanic medication not specified
Klein et al (1994)[38]	19 (33 full-term pregnancies for which complete data were available)	Structured interview to retrospectively assess course of panic disorder up to 1 year postpartum	74% (14)	21% (4)	5% (1)				22% (8) of the pregnancies involved first trimester antianxiety medication exposure; no second or third trimester exposure
Cohen et al (1996)[48]	10	Prospectively assessed women from 11 weeks' gestation to 9 months postpartum	10% (1)	80% (8)	10% (1)	10% (1)	70% (7)	20% (2)	90% (N = 9) took antipanic medication at some point during the perinatal period
Obsessive-compulsive disorder									
Williams and Koran (1997)[42]	29 (24 with at least 1 live birth)	Standardized telephone interview regarding clinical course of OCD during and after pregnancy with OCD outpatients	14% (4)	69% (20)	17% (5)			29% (7)	No information about medication use provided. 37% (N = 9) of women also reported a postpartum depression
Labad et al (2005)[44]	46 (12 with preexisting OCD and at least 1 live birth)	Semistructured interview regarding relationship between reproductive cycle events and OCD with female outpatients	8.0% (1)	83.3% (10)	8.0% (1)	0% (0)	50% (6)	50% (6)	No patients used antiobsessive treatment during pregnancy

[a]No studies have reported on the perinatal course of posttraumatic stress disorder or generalized anxiety disorder in women with preexisting disorder.
[b]Data in Pregnancy and Postpartum columns are expressed as percentage and number of women for the Cohen et al.,[46–48] Klein et al.,[38] and Labad et al.[44] studies and as percentage and number of pregnancies for all other studies.
Abbreviation: OCD = obsessive-compulsive disorder.

paniclike symptoms, including racing pulse, difficulty breathing, and generalized anxiety.[54] Medical evaluation, including assessment of thyroid function, hemoglobin levels, and blood pressure, is necessary, particularly in cases of new onset of anxiety during the perinatal period. Pheochromocytoma, a rare tumor of the adrenal gland, is also associated with symptoms of panic and generalized anxiety, as well as hypertension.[55] Unrecognized perinatal pheochromocytoma can have fatal consequences, as normal delivery can trigger hypertensive failure. Investigation for pheochromocytoma is therefore warranted in any woman with severe or symptomatic hypertension presenting with unusual features such as headache, palpitations, or excessive sweating. Diagnosis can be made using 24-hour urinary catecholamine assay for epinephrine, norepinephrine, and their metabolites. Scheduled cesarean delivery is usually necessary.[56]

A full review of safety issues related to medication exposure in utero and through breast milk is beyond the scope of this article. However, the data reported to date on potential effects of exposure of the developing fetus/breastfeeding infant to selective serotonin reuptake inhibitors (SSRIs) are largely reassuring.[57,58] It is important to note that untreated panic disorder could have negative effects on fetal development.[35,50] Findings from a study that examined the effect of an acute maternal stress response and anxiety on fetal heart rate in 17 healthy, third-trimester pregnant women indicated an increase in fetal heart rate patterns that could alter the neurobehavioral development of the fetus.[16] A careful risk-benefit assessment is therefore required in making treatment decisions during the perinatal period.[59]

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is characterized by intrusive thoughts or images, known as obsessions, and/or repetitive or ritualistic behaviors or thought patterns, known as compulsions. Typically, obsessions are anxiety provoking, whereas compulsions reduce anxiety, particularly when triggered by obsessions.[21]

OCD, more than other anxiety disorders, is thought to have a strong neurobiological basis, having been associated with cortico-striatal-thalamic-cortical circuits, and to be closely related to other neurologic conditions such as Tourette's syndrome. Perhaps as a result of this neurobiological basis, OCD is notable in that its symptoms vary little across time, culture, and age.[60] The sex difference in prevalence of OCD is small as compared to those for other mood and anxiety disorders. In at least one epidemiologic study, the difference was no longer statistically significant after controlling for sociodemographic differences between men and women (e.g., marital and employment status).[61]

Prevalence of perinatal OCD. Four studies have assessed the prevalence of OCD during the perinatal period (see Table 1).[19,20,23,24] The results suggest that the prevalence of OCD may be lower during pregnancy (0.2%–1.2%) than during the postpartum period (2.7%–3.9%). The DSM-IV reports an estimated lifetime prevalence of OCD in the general population of 2.5% and 1-year prevalence of 1.5% to 2.1%.[21]

Presentation and predictors of perinatal OCD. It has been extensively reported that obsessions in perinatal women often include fears of intentionally or accidentally harming the fetus or child.[43,62,63] In one recent retrospective study, over half (54%) of a sample of 17 women with OCD and at least 1 live birth reported obsessions or compulsions related to the fetus/newborn during pregnancy or the postpartum period.[44] An exception comes from a cross-sectional study of 47 postpartum women with symptoms of both depression and OCD whose thought content did not include infant harm.[24] Unlike other investigations (e.g., Jennings et al.[64]), this study did not include a structured tool specifically probing thoughts of infant harm. As a result, participants may not have felt comfortable reporting these thoughts to an unfamiliar interviewer when not directly queried.

Obsessional thoughts about harming the infant are not specific to OCD: they have been reported by over 40% of women with postpartum depression[64,65] and from 34% to 65% of new parents in volunteer community samples.[66,67] The prevalence of such intrusive thoughts across diagnoses and in healthy community samples suggests that at subclinical levels, they may be a normal feature of new parenthood. Evolutionary theories propose that these thoughts may be adaptive in that they may cause the parent to be vigilant in protecting the infant from potential harm.[68] These adaptive behaviors may trigger or increase obsessional symptoms in women with preexisting OCD or a genetic, neurologic, or cognitive vulnerability to OCD.[68]

It is important that OCD-related obsessions of infant harm be carefully differentiated from infanticidal ideation characteristic of postpartum psychosis and severe postpartum depression. The primary difference in clinical presentation relates to insight: women with OCD are typically aware that their symptoms are unreasonable, identify the thoughts as unwanted and separate from themselves (ego-dystonic), and go to great lengths to avoid acting on them.[68] There are no documented cases in the literature of women with "pure" OCD intentionally harming their infants. In contrast, women with postpartum psychosis, which affects only 0.1% of childbearing women,[69] typically lack insight, do not have fear or anxiety associated with the thoughts, and, if untreated, may act upon hallucinations or delusions that prescribe harming their children and/or themselves.[70] Women presenting with infanticidal ideation in the context of postpartum psychosis or severe postpartum depression require emergency psychiatric care to prevent such behavior. Women

with OCD in the absence of severe comorbid depression can be reassured that this condition has not been associated with infanticide in previous research.[71]

In contrast to obsessions, compulsive behaviors were not observed in perinatal women with OCD in early case reports or case series.[72] However, a more recent cross-sectional study of 84 postpartum women with either obsessions or compulsions found that compulsive handwashing or cleaning behavior was common and was often attributed to concerns that the infant would be exposed to contamination.[24] Women who reported other types of compulsive behaviors (e.g., checking or counting) either did not meet diagnostic criteria for OCD or reported that they had engaged in these behaviors prior to the birth of the child.[24]

Infant-focused symptoms of OCD could have important implications for development of the mother-infant relationship. Some women who fear harming their infants are reported to modify their behavior with their children, in some cases resulting in an inability or refusal to care for them.[62,64,72] In one study of 7 women with postpartum OCD, 5 women (71%) reported dysfunctional maternal behavior, including avoidance of or fear of separation from the infant/child.[63] Disorders of the mother-infant relationship have been reported in 10% to 25% of women referred to psychiatrists following childbirth.[73] Although the concept of impaired mother-infant interaction is controversial and to date is not recognized as a disorder in the DSM-IV, risk for child neglect and psychiatric or learning disorders has been reported among children whose mothers exhibit impaired maternal behavior.[74]

Case reports suggest that comorbid depression is common among perinatal OCD patients, evolving approximately 2 to 3 weeks following onset of OCD symptoms.[63,72] However, a cross-sectional study of a community sample of 147 women found that comorbid depression was present in less than half of the participants with syndromal or subsyndromal OCD.[19] This was contrasted with comorbidity rates of 50% or greater among women with panic disorder or generalized anxiety disorder (GAD).[19]

Personal psychiatric history may also be associated with OCD. One retrospective study of 17 OCD patients with at least 1 live birth found that those with postpartum onset or worsening of OCD were more likely than those without postpartum onset or worsening to have a history of major depressive disorder.[44] Premenstrual depressive mood was also significantly associated with both postpartum onset and worsening of OCD, suggesting a common vulnerability to psychiatric symptoms related to the premenstrual and perinatal periods.[44]

An early retrospective study of 16 women with children suggested an association between perinatal OCD and preterm delivery, postterm delivery, and delivery by cesarean section without labor.[40] A more recent retrospective study of 17 women who had given birth to a live child found that none of the clinical or obstetric variables examined, including being primiparous, type of delivery, and pregnancy, delivery, or postpartum complications, were associated with onset or an increase in OCD symptoms during the postpartum period.[44]

New onset of OCD. Several studies have investigated the extent to which women with OCD report the onset of their illness to be associated with pregnancy or childbirth (summarized in Table 2). Studies of new-onset perinatal OCD have been retrospective and uncontrolled and therefore subject to remembering or reporting bias. However, results indicate that as many as 40% of childbearing OCD outpatients have onset during pregnancy,[41–44] and up to 30% have onset during the postpartum period.[43,44] These findings are supported by numerous case reports.[62,63,72]

Course of preexisting OCD. Only 2 studies have assessed the course of OCD across the perinatal period (Table 3). In the larger study, 57 women outpatients with OCD were interviewed retrospectively regarding the course of their illness in relation to reproductive events; 38 of these women had been pregnant, and 31 had delivered at least 1 child.[42] Of the 29 women with preexisting OCD who became pregnant, the majority (N = 20, 69%) reported no change in their symptoms during pregnancy, whereas those who reported a change were approximately equally distributed between improvement and worsening. Seven (29%) of the 24 women with a full-term live birth reported postpartum exacerbation of symptoms.[42] The same general pattern of findings was also observed in a more recent study including 12 OCD patients with at least 1 live birth.[44]

Treatment of perinatal OCD. As with panic disorder, no controlled studies have been conducted to examine effectiveness of treatment methods for perinatal OCD. Case reports provide preliminary evidence that SSRIs and behavior therapy, either independently or in combination, are most likely effective.[43,62,63,72,75] One open-label study found that quetiapine augmentation was an effective management strategy for postpartum OCD among 11 of 14 women who were nonresponders to SSRI or serotonin-norepinephrine reuptake inhibitor monotherapy.[76]

For OCD outside of the perinatal period, the SSRIs have been shown to be effective and well tolerated. There is also empirical support demonstrating that cognitive-behavioral approaches, administered either individually or in groups, can control OCD symptoms.[60] Until further data are available, perinatal OCD is best managed in the same manner as OCD in the general population. However, potential effects of medications on the fetus/breastfeeding infant are a consideration.[71]

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is an anxiety disorder characterized by exposure to a traumatic event

appraised by the individual as one that could involve actual or threatened death or serious injury or a threat to the physical integrity of self or others (criterion A1).[21] Moreover, the person's response to the stressor involves intense fear, helplessness, or horror (criterion A2).[21] Symptoms of PTSD include reexperiencing of the traumatic event, such as intrusive recollections or recurrent and distressing dreams of the event; avoidance of stimuli associated with the trauma and numbing of emotional responsiveness; and hyperarousal, such as difficulty sleeping and concentrating and irritability. PTSD is acute if the duration of symptoms is less than 3 months and is chronic if symptoms persist beyond 3 months.[21] Although the DSM-IV does not specifically identify childbirth as an example of an extreme stressor, reports suggest that childbirth can qualify as a traumatic event that results in PTSD in some women.[77]

Prevalence of perinatal PTSD. PTSD has been recognized as occurring after stressful medical and surgical procedures that involve intense pain,[78] invasive medical procedures,[79] and obstetric and gynecologic procedures,[80] suggesting that it is also relevant to consider traumatic labor and birth experiences as potential stressors for PTSD symptoms.[81] For example, in a retrospective cross-sectional study, 500 volunteer participants were recruited through advertisements, and of the total sample, 20% described having undergone at some point, at least 1 month previously, an obstetric or gynecologic procedure that they considered very distressing or terrifying and out of the range of normal experience.[80] The 20% who reported distressing procedures were then recontacted and asked to complete the measure for PTSD diagnosis (PTSD Interview[82]). Results indicated that 30 respondents (6%) met diagnostic criteria for PTSD, suggesting that women who experience traumatic obstetric and/or gynecologic procedures may develop PTSD. Reliance on self-report of retrospective data is a limitation of this study, although the use of a standardized measure helps to attenuate this concern. Furthermore, additional follow-up of the 6% of participants who met acute PTSD criteria may have contributed information as to those who went on to meet chronic PTSD criteria.

Studies that have assessed the prevalence of PTSD associated with the perinatal period are summarized in Table 1. A variety of assessment measures have been applied to this population to diagnose prevalence of PTSD and PTSD symptoms in the postpartum period. The inconsistency in assessment measures, and in particular the absence of differentiation between clinical PTSD and PTSD symptoms, may in part explain the wide range of prevalence values (0%–6.9%) reported. Two studies have investigated prevalence of PTSD among pregnant women, yielding rates of 2.3%[26] and 7.7%.[25] The DSM-IV reports prevalence rates for community-based populations for PTSD ranging from 1% to 14%, with variability related to methods of measurement and the population sampled. Two studies have reported that approximately 25% of their perinatal samples were partially symptomatic for PTSD.[28,29] However, use of the term *PTSD symptoms* in the literature is problematic and may mislead one to conclude this to be a diagnosis of PTSD. PTSD symptoms, however, may resolve and be more like an acute stress response or disorder. A further limitation to the studies reviewed is the single assessment time: the lack of longitudinal follow-up limits our knowledge of the trajectory and course over time of those who do meet criteria for acute PTSD, chronic PTSD, or PTSD symptoms.[19,20,77,78]

Presentation and predictors of perinatal PTSD. Perinatal PTSD has been associated with some distinct clinical features, including avoidance of the baby/impaired mother-infant relationship, sexual dysfunction, and avoidance of future childbearing. Case reports describe women who avoided sexual involvement with their partners because sexual activity resulted in reexperiencing of the pain and distress experienced during traumatic labor.[83] PTSD occurring after childbirth may lead to postponement or avoidance of future childbearing,[83] or requests for planned cesarean sections in an attempt to avoid retraumatization by childbirth.[84,85] Requests for termination of an unplanned pregnancy[86] and sterilization[83] have also been documented.

Case reports and qualitative studies have described women with PTSD-type reactions who avoided contact with their infants, sometimes for several years, as a result of a childbirth experience perceived as traumatic.[77,87–89] In these cases, the child may be a stimulus for reexperiencing of the traumatic delivery. Similarly, qualitative research indicates that some women may avoid not only their own infant, but also other mothers and babies following a traumatic childbirth experience,[77] resulting in increased maternal isolation.

Previous mental health history, and particularly a history of major depression or generalized anxiety disorder, has been associated with risk for PTSD.[25,30,31] Although PTSD and depression may frequently be comorbid in the perinatal period,[19] researchers have reported that postnatal PTSD and depression also occur in the absence of one another.[30,90] In a cross-sectional study, 6 of the 8 women identified as meeting criteria for PTSD had elevated scores indicative of depression on the Edinburgh Postnatal Depression Scale. Both trait anxiety[30] and anxiety sensitivity[91] have also been associated with risk for PTSD.

Recent and childhood experiences of trauma have been associated with PTSD in the general population,[92] but few studies have investigated these variables in relation to perinatal PTSD. Studies of perinatal women have found an association between experiencing 2 or more previous traumatic life events and risk for perinatal PTSD.[25,93] In a convenience sample of trauma-exposed pregnant women,

very high rates (58%) of PTSD were identified.[94] Finally, a cross-sectional study of 31 Cambodian mothers in Australia found that the number of pre-migration traumas experienced or witnessed was significantly associated with PTSD symptoms.[95] The types of trauma associated with perinatal PTSD in these studies have been variable. In one study, PTSD symptom scores were highest among women who reported partner-related traumatic events.[94] Another study found that the most commonly reported traumas among women with PTSD were the unexpected death of a close friend or relative and having something terrible happen to a close friend or relative.[25]

Childhood or adulthood sexual assault can also be associated with perinatal PTSD. Loveland Cook et al.[25] reported that 50.9% and 35.1% of subjects with PTSD in their sample of economically disadvantaged pregnant women reported sexual assault by a nonrelative and relative, respectively, and that 36.8% of the sample experienced the traumatic event that precipitated PTSD prior to the age of 15 years. These results are consistent with research indicating high rates of childhood abuse among women seeking treatment for perinatal depression.[96,97] Women with a history of sexual abuse may experience triggering of memories of abuse in response to childbirth procedures. This may result in avoidance of necessary medical procedures (e.g., internal examination).[92,98]

A potential relationship between type of delivery and postpartum PTSD has received inconsistent support in the literature. One prospective study measured PTSD symptoms 6 weeks after delivery in 40 women who had given birth in one of 4 manners: spontaneous vaginal delivery, induced vaginal delivery, instrumental vaginal delivery (involving assisted delivery by forceps with an unexpected episiotomy under local anesthetic), or emergency cesarean section. Women who underwent instrumental deliveries endorsed more PTSD symptoms than did women who underwent spontaneous vaginal delivery or cesarean section.[99] A similar prospective study compared the incidence of PTSD in 326 women undergoing normal vaginal delivery, instrumental delivery, elective cesarean section, or emergency cesarean section. At 4 weeks postpartum, mothers who had undergone an emergency cesarean delivery and those who had instrumental vaginal deliveries reported significantly more PTSD symptoms than those who had had either elective cesarean sections or spontaneous vaginal deliveries.[100]

In contrast, a third study of 40 women found that those who delivered by elective cesarean section had higher anxiety and PTSD scores than those who had spontaneous vaginal deliveries or emergency cesarean sections.[91] Finally, the largest study of this question (N = 1550) found that women who underwent emergency cesarean section or instrumental deliveries were 6.3 times and 4.8 times, respectively, more likely than women who underwent spontaneous vaginal deliveries to meet criteria for PTSD at 4 weeks postpartum.[122] However, the authors note that numerically more women with normal vaginal deliveries than with emergency cesarean section or instrumental deliveries met criteria for PTSD in their sample, suggesting that characteristics of both the birth event and the individual are relevant in determining risk for postpartum PTSD. Appraisal of the childbirth experience as traumatic may be a better predictor of PTSD than type of delivery.[77]

Other aspects of the birth experience besides type of delivery may contribute to risk of PTSD, including pain[80,90,91,101] and powerlessness or lack of control[30,31,80,101] during labor and delivery. Perceived quality of the intrapartum care provided by medical personnel has been associated with PTSD symptoms.[80,91] In Beck's phenomenological study of birth trauma, perceived lack of communication by labor and delivery staff contributed to the appraisal of a traumatic birth.[77] Perceptions of low levels of social support from hospital staff have been related to PTSD symptoms in both qualitative and quantitative studies,[30,31,101] as has lack of support from the woman's partner during the birth.[30]

Finally, maternal and infant complications have been associated with perinatal PTSD. For example, higher levels of PTSD symptoms have been reported among mothers of premature infants than among mothers of healthy, full-term infants.[102] Preeclampsia has also been associated with risk for PTSD.[103,104]

New onset of PTSD. Only 1 study has prospectively assessed incidence of PTSD across the perinatal period.[27] This study included an assessment in late pregnancy and as such demonstrates the first evidence of new-onset PTSD following childbirth. As summarized in Table 2, 3.2% of the sample showed onset of PTSD by 6 weeks postpartum. Further, the authors identified a small but significant proportion of women (1.5%) who developed chronic PTSD (i.e., PTSD persisting for 3 months or more).[27]

Course of preexisting PTSD. No studies have reported on the course of PTSD in perinatal women with preexisting disorder.

Treatment of perinatal PTSD. No published studies have evaluated treatment interventions for perinatal PTSD. However, some efforts have been made to prevent PTSD among women assessed as having had a traumatic childbirth using critical event debriefing. This prevention strategy involves talking about the traumatic experience with a trained professional: both validation and accommodation of the traumatic event may be facilitated. Debriefing interventions for perinatal PTSD are supported by evidence from qualitative studies that women who perceive childbirth to have been traumatic express a desire to discuss and analyze their experiences at length.[77,101]

Early studies of critical event debriefing with perinatal populations yielded conflicting results, both when debriefing was used to attempt to prevent PTSD[100,105] and

when it was used to prevent postpartum depression.[106,107] In fact, in the well-designed study by Small and colleagues,[107] women who were randomly assigned to receive a midwife-led debriefing session after an operative delivery had increased rates of maternal depression at 6 months postpartum. However, a more recent study found that a debriefing-modeled counseling intervention was effective in reducing risk of trauma symptoms and depression at 3 months postpartum.[108] Several notable features in the design of this intervention may have contributed to the positive results. First, women were selected for participation in the study by interviewing them within 72 hours of birth to determine if they met criterion A of the DSM-IV criteria for diagnosis of PTSD. As such, participants were only included in the study if they perceived their childbirth experience to have been traumatic, rather than on the basis of having had an operative delivery, as was typically done in previous debriefing studies. Further, the counseling intervention administered in this study consisted not only of face-to-face debriefing in the immediate postpartum period, but also telephone counseling at 4 to 6 weeks postpartum.[108] This design is consistent with findings from the general PTSD literature that a single debriefing session immediately following a traumatic event may be ineffective in preventing PTSD and may in fact cause harm.[109] The recent promising results suggest that further research is warranted to examine the potential for prevention of perinatal PTSD using debriefing-style counseling interventions.

Generalized Anxiety Disorder

Generalized anxiety disorder is a chronic condition characterized by at least 6 months of frequent worry, together with additional symptoms including poor concentration, muscle tension, fatigue, and restlessness.[21] GAD affects approximately 5% of the general population.[110]

According to DSM-IV criteria, symptoms of GAD are required to be present for 6 months before a diagnosis can be made,[21] and therefore diagnostic criteria for new-onset GAD are unlikely to be met during either the 9 months of pregnancy or the early postpartum period. Further, unlike the other anxiety disorders, onset of GAD in women typically occurs past age 35[110] and therefore may postdate childbearing for many women. Adjustment disorder with anxiety is usually the appropriate differential diagnosis during the perinatal period. Adjustment disorder with anxiety is characterized by the same symptoms as GAD, but the symptoms occur in the context of a stressful life event (e.g., pregnancy or childbirth) and last no longer than 6 months from the time of this event.[21,111]

Prevalence of perinatal GAD. Only 1 study has estimated the prevalence of GAD during pregnancy, reporting a rate of 8.5% during the third trimester of pregnancy.[20] Three studies have estimated the prevalence of GAD or adjustment disorder with anxiety during the postpartum period, yielding rates of 4.4% to 8.2% (see Table 1).[19,32,33] The range in sample size (68–148 participants) may explain some of the variability in the estimates. The DSM-IV reports a 1-year prevalence rate for GAD of approximately 3% in a community sample and a lifetime prevalence rate of 5%,[21] suggesting that GAD/adjustment disorder with anxiety may be more common in postpartum women than among the general population.

Presentation and predictors of perinatal GAD. It can be difficult to differentiate GAD from normal, nonpathologic anxiety, since worries about the health of the fetus or anticipation of a painful delivery are common among healthy perinatal women.[112] In one study, a "Pregnancy Experiences Scale" was developed and administered to a sample of nearly 200 women in the second and third trimesters of pregnancy.[113] The most frequently endorsed hassles were discomforts of pregnancy, inability to do tasks/chores, and clothing/shoes not fitting. Thoughts about labor and delivery and whether the baby was normal were endorsed by 80% and 76% of the sample, respectively. It should be noted that uplifts (positive experiences), including how much the baby is moving and visits to the obstetrician/midwife, were endorsed more often and with greater intensity than were hassles. Women who reported greater hassles also reported greater uplifts, indicating that personality variables may influence how normal pregnancy-related events are interpreted.[113] Domains of worry have also been assessed among postpartum women: in one study, a "Postpartum Worry Scale" was developed and administered to a sample of 68 women at 8 weeks postpartum. Worries about finances, the participant's appearance, household duties, and the cleanliness of surroundings were most frequently endorsed.[114]

No studies to date have compared the content and nature of worry in women with GAD to that in healthy perinatal women. In the general population, GAD is distinguished from normal worry on the basis of 3 characteristics: in GAD, worry is excessive and interferes with daily functioning; worry is widespread, usually to multiple domains of the person's life; and worry can occur without any identifiable trigger.[21] These same characteristics may be helpful in differentiating perinatal GAD from normal anxiety as well. It has been recommended that perinatal worry be further investigated when a woman is worrying more than other perinatal women, when she cannot be reassured or cannot control the worry, or when excessive and uncontrollable worry has persisted for 6 months or more.[34]

No studies have reported on risk factors for or predictors of GAD in the perinatal period. However, 1 cross-sectional study has described correlates of anxiety symptoms in perinatal women. Wenzel et al.[19] found that personal psychiatric history, family psychiatric history, and socioeconomic status were significantly associated

with anxiety symptoms assessed using the Beck Anxiety Inventory. Additional research is needed to determine whether these variables are predictive of clinically significant anxiety disorders.

New onset of GAD. As described above, new onset of GAD is unlikely during the perinatal period, due to the duration criterion for the diagnosis. None of the studies of perinatal adjustment disorder with anxiety have conducted baseline assessments to determine whether symptoms began during the perinatal period or were preexisting. In their cross-sectional study of postpartum anxiety disorders, Wenzel et al.[32] reported that 2 of the 3 women who met diagnostic criteria for GAD described subsyndromal worry prior to pregnancy or childbirth; the third woman reported a history of clinically significant GAD symptoms prior to pregnancy. Research is therefore needed to establish whether the perinatal period is associated with new-onset GAD and/or adjustment disorder with anxiety.

Course of preexisting GAD. No studies have examined the course of preexisting GAD across the perinatal period.

Treatment of perinatal GAD. No studies have investigated treatment of perinatal GAD; however, there is evidence for the effectiveness of cognitive-behavioral therapy, SSRIs, and benzodiazepines in the general population of GAD patients.[115] As with panic disorder, careful assessment is required to rule out potential medical causes of anxiety symptoms before treatment is initiated. If pharmacotherapy is used, antidepressant medications are preferred over the benzodiazepines due to their better safety profile for the developing fetus and/or breastfeeding infant.[58,116]

CONCLUSIONS AND FUTURE RESEARCH DIRECTIONS

This review is limited by the quality of the available research evidence. To date, few studies have examined prevalence of perinatal anxiety disorders as defined by diagnostic criteria,[21] and no studies have included appropriate non-perinatal control groups. The measures used to assess anxiety have varied considerably from study to study and do not always conform to DSM diagnostic criteria. For example, in the case of PTSD, it is necessary to distinguish among appraising a birth as being traumatic, experiencing an acute traumatic stress response (e.g., symptoms of intrusion and/or avoidance), and clinically meeting the DSM-IV criteria for a diagnosis of PTSD.

The studies that have reported on prevalence of perinatal anxiety disorders are typically based on small, selected samples (such as women participating in an intervention trial or women reporting symptoms of depression). In most cases, only women who met certain screening criteria, and not the total sample, were interviewed with structured diagnostic interviews. This could have resulted in underestimates of prevalence due to missed cases among the portion of the sample that was not interviewed. In spite of these limitations, however, it is notable that the literature reviewed suggests higher prevalence of OCD and GAD in women during the prenatal and/or postpartum period than in the general population.[21] Further, appropriately controlled studies are needed to confirm this finding.

Available evidence suggests that unique clinical features of perinatal anxiety disorders could have important implications for the mother-infant relationship[35,63,77]; however, these data are largely derived from case reports and qualitative studies. The prevalence and precise nature of these disruptions remain unclear and underinvestigated. Further systematic investigation of the potential impact of perinatal anxiety disorders on infant development and mother-infant attachment is needed.

Very limited data are available to guide clinical interventions for women with or at risk for perinatal anxiety disorders. It has been presumed that treatments for panic disorder, OCD, and GAD will be as effective during the perinatal period as they are outside the perinatal period, but research is needed to confirm that this is so. Data are conflicting with respect to the effectiveness of critical debriefing strategies in the prevention of PTSD, and no empirically based clinical interventions are available as standard of care. Further research to identify empirically validated intervention protocols is required to ensure quality and consistency of care for women with perinatal anxiety disorders.

Anxiety symptoms and disorders may also develop in women with fertility problems and those who experience a pregnancy loss.[117] Similarly, there is some evidence that new and prospective fathers and partners may develop anxiety disorders.[118,119] More research is needed to further elucidate the risk for anxiety disorders in these populations.

The literature identified for this review includes few prospective, longitudinal studies. As such, few studies have examined whether the anxiety disorders predate childbirth. Causal factors for anxiety disorders that predate pregnancy may be very different than those for anxiety disorders with perinatal onset.[120] Future research should screen for both current and lifetime anxiety disorders. Longitudinal studies will also allow for better assessment of time of onset for perinatal anxiety disorders (i.e., to determine times within the perinatal period when risk of onset is highest).

In conclusion, the limited available research indicates that anxiety disorders are common during the perinatal period. The high prevalence of these disorders, and particularly of OCD and GAD, indicates a potential role for screening. As has been described in the literature on perinatal depression, providers of obstetric care are most

likely ideally placed to perform the necessary screening and assessment due to their frequent contact with women across the perinatal period.[121] Considering the lack of adequate psychometric data regarding the use of existing anxiety scales in perinatal populations, there may be a need to develop accurate, acceptable, and feasible screening tools for perinatal anxiety disorders. Finally, due to the complexity of anxiety disorders in this population, and the potential for impact on the fetus/infant, the importance of multidisciplinary team approaches in provision of psychiatric care is evident.

Drug names: imipramine (Tofranil, Surmontil, and others), quetiapine (Seroquel).

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, imipramine is not approved by the U.S. Food and Drug Administration for the treatment of perinatal panic disorder, and quetiapine is not approved for perinatal obsessive-compulsive disorder.

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Women's Mental Health section. Please contact Marlene Freeman, M.D., at marlenef@email.arizona.edu.

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