Recognizing and Managing Postpartum Psychosis

A Clinical Guide for Obstetric Providers

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KEYWORDS

• Postpartum psychosis • Bipolar disorder • Perinatal psychiatric disorders
• Treatment

KEY POINTS

- Postpartum psychosis (PPP) is a rare psychiatric emergency that can endanger the lives of the mother and child.
- It most often arises within 10 days of childbirth and is characterized by bizarre thoughts and/or behavior, alterations of consciousness, and mood fluctuation.
- The single biggest risk factor is a personal history of bipolar disorder, and most women with PPP will go on to develop bipolar disorder.
- It carries high rates of suicide and infanticide, and suspected cases require psychiatric evaluation as soon as possible.
- Treatment requires hospitalization and aggressive pharmacologic management.

INTRODUCTION

Postpartum psychosis (PPP) is at once the most dangerous and the least understood of perinatal psychiatric disorders. It affects 1 to 2 per 1000 women and constitutes a true psychiatric emergency, one that requires immediate hospitalization and treatment.[1,2] The lack of knowledge about what it is, how to recognize it, and how to treat it, combined with stigma about perinatal psychiatric disorders in general and the lack of appropriate treatment venues, means that it is often missed, by both obstetricians and psychiatrists, with sometimes tragic consequences.

PPP has been noted since antiquity. Hippocrates described the first case known to the medical literature in 400 BC; his patient was delusional, confused, and had

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insomnia within 6 days of a twin birth.[3] A medieval gynecologist attributed the disorder to "too much moisture in the womb, causing the brain to fill with water."[4] By the late eighteenth century, German and French obstetricians and neurologists were beginning to write more frequently about the disease. In 1858, French psychiatrist Louis Victor Marcé[5] published his *Treatise on the Madness of Women who are Pregnant, Recently Delivered, or Nursing*.[5] Marcé's carefully observed treatise, although suggesting treatments that today seem woefully barbaric (applying leeches to the vulva, for example), is a model of observation; Marcé saw in his postpartum mothers the same symptoms that doctors struggle to control today. His observations led him to conjecture about the role of the immune response and the endocrine system, 2 systems that today are widely acknowledged to contribute to postpartum mental illness.

CLINICAL PRESENTATION

The name PPP is not, perhaps, the best moniker for an illness that is at least as much an affective, or mood, disorder as it is a psychotic disorder. Many clinicians mistakenly think that the term can be applied to any psychotic symptoms in the postpartum period or that its clinical features will be identical to those of schizophrenia or other primary psychotic disorders. In fact, the symptoms of PPP are distinctive and unique. The onset is typically sudden and occurs within the first 2 weeks post partum.[6–8] The literature has frequently described the distinctive clinical features (**Box 1**), which include a delirium-like waxing and waning of consciousness, disorganization and confusion, depersonalization, and bizarre delusions (often concerning the child or childbirth). Early warning symptoms include insomnia, anxiety, irritability, or mood fluctuation. Although the psychotic symptoms are often the most dramatic manifestation, women also present with mood symptoms: mania (can be irritable or elevated), depressive symptoms, or mixed symptoms. A recent clinical cohort study tracked the phenotypic characteristics of 130 consecutive cases of PPP and used latent class analysis to describe 3 separate symptom profiles:

1. Cases characterized by mania and/or agitation, with irritability much more common than elevated mood (34%)
2. Cases characterized by depression and/or anxiety (41%)
3. Cases showing an atypical or mixed profile (25%)[9]

Across all cases, 25% of patients were disorganized, 20% disoriented, 10% had disturbed consciousness, and 5% developed catatonia. Seventy-two percent had abnormal thought content, which most often consisted of persecutory delusions; a minority had frank hallucinations. See **Boxes 2–4** for representative clinical case presentations.

Box 1
Clinical features of postpartum psychosis

- Disorganization
- Confusion
- Depersonalization
- Insomnia
- Irritability
- Abnormal thought content (delusions and/or hallucinations)
- Abnormal mood (mania or agitation, depression, mixed)

Box 2
Clinical case presentation 1

Postpartum psychosis with manic features

Ms A was a high-achieving professional with no prior psychiatric history who had a twin birth 12 days before her psychiatric presentation. Her babies had been born at term by a planned cesarean delivery because of chorioamnionitis; antibiotic therapy was successful, and she left the hospital on time 4 days after the birth. She slept very little in the hospital and was noted by the nurses to be extremely vigilant about the babies and mildly anxious. Her family reported that she did not sleep at all for 6 days following her hospital discharge. She expressed great anxiety about arrangements at home (worrying about clothes, diapers, and the like) and about the ability of other family members to manage the twins. She was exclusively breastfeeding until 2 days before presentation, when her family dissuaded her from breastfeeding in the hope that she would be able to sleep more; the intervention did not help. On the day of presentation, she began to be suspicious of several family members, accusing them of poisoning the babies' bottles, and began to hide the bottles in secret locations around the house. When her mother suggested that they drive to the hospital, the patient bolted from the car into traffic and was found several hours later by a police officer who drove her to the emergency department. On arrival, the patient was oriented to her name and the date but was unsure where she was, spoke very quickly and was uninterruptable, and talked loudly about the cameras she was sure were watching her in the emergency department and about the physicians, whom she thought were in league with her family to poison the infants.

CAUSE AND RISK FACTORS

PPP is one of the few psychiatric disorders with a clear biological trigger: childbirth. The nineteenth-century psychiatrists who first described it (Esquirol[10], Marcé[5]) noted that symptoms were often associated with pregnancies that had gone awry because of infection, preeclampsia (PE), hypertension, or other medical problems[5]; but more

Box 3
Clinical case presentation 2

Postpartum psychosis with depressed features

Ms B was a sheltered young woman from an insular immigrant community. She had experienced childhood trauma and had a known history of depression and anxiety, successfully treated with antidepressants in the past. She had been well throughout her pregnancy, on no medication; but within 5 days of an uncomplicated spontaneous vaginal birth she became disoriented at home and was unable to find her way from her bedroom to the living room. Over the next several days, her family reported that she moved very slowly and seemed confused; she had a poor appetite, did not seem to understand how to hold or care for the baby, and spent much of the day lying in bed but did not seem able to sleep. She began to make worrisome statements, such as "I'm not here" and "I didn't have a baby." The patient's general practitioner prescribed an antidepressant, which did not help her symptoms; the patient became increasingly confused and unable to complete daily activities, such as showering and eating. The family took over the care of the baby and assigned a family member to care for the patient at home. Several weeks later, the situation had not improved; the family presented to a psychiatrist. The patient was oriented to her name only; she could not name the season or what type of building she was in; she clung to her sister's hand and was unable to find the door of the room she was in. When she was asked about her baby, the patient stated "I don't have a baby, I'm not married."

Box 4
Clinical case presentation 3

Postpartum psychosis with mixed features

Ms C was an elementary school teacher who was quite knowledgeable about mental health. She had no prior psychiatric history but had 2 first-degree relatives with bipolar 1 disorder, one of whom had had multiple hospitalizations and was eventually stabilized on lithium. Her pregnancy was uneventful; but labor lasted more than 36 hours and ended in an emergency cesarean delivery, which the patient found traumatic. Two days after discharge, she represented to the hospital stating she had had a panic attack in the middle of the night and was unable to sleep; this was her first panic attack. The overnight resident deemed her anxious but stable, treated her with lorazepam, and discharged her. She represented several hours later complaining of continued insomnia and anxiety. The consulting psychiatrist could elicit no symptoms of frank mania or psychosis but was concerned about her anxiety, insomnia, and family history of bipolar disorder. Upon discharge she was prescribed lorazepam 3 times daily and was referred to a perinatal psychiatrist who would see her twice weekly. At her second outpatient visit, the patient reported that she was now sleeping 6 hours nightly but continued to feel anxious. The psychiatrist started sertraline at 25 mg. Two days later, the patient's partner called the psychiatrist stating that the patient was writhing on the floor complaining of bugs crawling over her skin and had been agitated and pacing just before. By the time the patient arrived in the emergency department for evaluation, she was mute and catatonic.

recent studies have been inconclusive about whether medical factors in pregnancy consistently predict the risk for the disorder, with several studies finding that no pregnancy-related or obstetric factors offer a heightened risk for PPP[11–14] and others finding some specific risks.[15–17]

Parity

Numerous studies have found a higher risk for PPP in primiparous women.[13,15,17–19] Although some of that risk may exist because some women who experience PPP do not have further children (in one recent study, only 45% went on to have subsequent pregnancies),[16] that fact does not entirely explain the risk, for even those that restrict analysis to women who have had more than one pregnancy find a consistent risk for primiparous women.[15] Some of this risk may be due to the increased psychosocial stress of a first child, but some may also be due to unknown biological factors. Research has not yet illuminated whether time between pregnancies, pregnancies with different fathers, or sex of the fetus may affect a woman's risk; but these would be interesting areas to explore given the emerging literature on these areas for other pregnancy morbidities.[20–22]

Personal History of Bipolar Disorder

The strongest single risk factor for PPP is a personal history of bipolar disorder, with 20% to 30% of parous women with known bipolar disorder experiencing PPP.[23] Yet in a recent large study only 33% of women presenting with PPP had a prior psychiatric history, and of those only one-third had been diagnosed with bipolar disorder.[16] Although there is increasing evidence that some women with PPP will experience only puerperal episodes, most women who present with PPP as their first psychiatric episode will eventually meet the criteria for bipolar disorder, with one comprehensive study showing a risk of a subsequent nonpuerperal episode of 69%. A presentation of

PPP should, therefore, be considered bipolar disorder and treated as such until proved otherwise.

Family History/Genetic Factors

Although no specific genes that contribute to risk have been identified, there is strong evidence that puerperal psychotic episodes run in families.[24–26]

Preeclampsia

The clinical features and risk factors for PE overlap with those of PPP, including the strong risk of primiparity and the high risk of subsequent episodes. Evidence so far is inconclusive, however, with some studies finding no increased risk for PE in women with PPP.[27] One recent registry-based study did find a strong relationship between PE and first-onset postpartum psychiatric episodes, with an odds ratio approaching 5 in primiparous women, but did not distinguish between PPP and other types of postpartum psychiatric disturbance.[28] This subject remains an intriguing area for further research.

Sleep Disturbance

Sleep loss has long been recognized as a trigger for mania; in fact sleep deprivation can be used as an effective, if drastic, treatment of depression.[29–35] There has been very little research specifically on sleep deprivation and puerperal manic or psychotic episodes, though there has been an association noted between women who have longer labors or give birth in the middle of the night and the subsequent development of PPP.[36,37] A recent study found that women with known bipolar disorder who report that sleep disturbance is a common trigger for their manias are at heightened risk for episodes of PPP.[38] This finding was specific to PPP (as opposed to postpartum depression [PPD]) and indicates that future research in this area is warranted.

Immune Dysregulation

Perhaps the most intriguing recent evidence about the biological origins of PPP is the evidence for immune system dysregulation. Bergink and colleagues[39] have explored several areas of immune dysfunction in PPP[40] and found evidence for increased rates of autoimmune thyroiditis (present in 19% of subjects with PPP and only 5% of controls)[41] as well as failure of normal T-cell elevation, increased monocyte to nonmonocyte ratio, and significant upregulation of immune-related genes in subjects with PPP.[39,40] Kumar and colleagues[42] examined immune cell types by flow cytometry and found significant alterations in the number and type of T cells and natural killer cells in women with PPP. This subject is one of the most active areas of biological research on PPP.

Hormonal Change

Although the precipitous drop in estrogen and progesterone in the 24 hours following childbirth is a tempting candidate for the cause of postpartum psychiatric disorders, most studies have shown little difference in absolute levels of reproductive hormones between healthy women and those experiencing psychiatric symptoms.[43,44] Instead, certain women seem to have a vulnerability to hormonal fluctuation.[45] There has been very little research on hormonal contributors to PPP specifically. There have been case reports of women with PPP who have hypoparathyroidism[46] and Sheehan syndrome[47] and of the role of melatonin.[48] Some small trials and case reports have examined estrogen and progesterone for

prevention or treatment of PPP, with mixed results for estrogen and no good evidence to support the use of progesterone (as summarized by Doucet and colleagues[49] in 2011). Although further research is clearly needed, at this time the evidence does not support the use of hormones either to treat or to prevent PPP.

SCREENING AND ASSESSMENT

There is no standardized set of questions or screening tool for PPP, and the diversity of presentation makes it difficult to create an algorithm for screening. The widely used Edinburgh Postnatal Depression Scale,[50] a 10-item self-report screen for PPD, will pick up symptoms of depression or anxiety; but it cannot distinguish between unipolar and bipolar depression nor can it assess symptoms of psychosis. There is also no completely standard set of laboratory tests because of the rarity of the disorder, but evidence about the biological cause has grown enough at this point to suggest a likely set of laboratory tests. **Boxes 5** and **6** outline the most important screening questions and laboratory tools.

DIFFERENTIAL DIAGNOSIS

PPP is one of 3 affective (mood) syndromes that can affect women in the postpartum. The baby blues affect 85% to 90% of women.[51–53] This syndrome is a self-limited syndrome of mood lability (up or down), tearfulness, and feeling overwhelmed, but without serious effects on the woman's functioning. It occurs within days of birth and is generally resolved within 2 weeks. It is unrelated to psychiatric history and requires no intervention other than support. PPD is a more serious disorder that can include low mood, anhedonia, and sometimes suicidality. It affects 10% to 20% of postpartum women.[54] The *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) defines it as a depressive episode "with peripartum onset,"[55] beginning in the third trimester or within 4 weeks post partum. Symptoms must last at least 2 weeks to qualify as a depressive episode; but any woman whose symptoms are severe and affect functioning and/or is suicidal, unable to function, or exhibits suicidality should be suspected of likely depression even if that time criterion has not been met. Although it often begins within the *DSM*-specified time period, many women will not present until later in the postpartum course. Women with PPD are often anxious[56]; postpartum women can also present with generalized anxiety disorder, a condition in which patients worry excessively about things across many domains of life.

Box 5
Important screening questions for patients and/or families

- Is this the patient's first psychiatric presentation?
- If she has a psychiatric history, is it of depression, mania, or both?
- Is there any family history of bipolar disorder?
- Has the patient been using any substances?
- Does the patient have thoughts of harming herself or the child? It is important to ask this in a nonjudgmental fashion: It can be very overwhelming to be a new mother. Sometimes women have scary thoughts; they might think about hurting themselves or hurting their babies. Has that ever happened to you?

Box 6
Important assessment tools

- Complete physical examination
- Neurologic examination
- Comprehensive metabolic panel
- Complete blood count
- Urinalysis
- Urine toxicology screen
- Thyroid stimulating hormone, free thyroxine (T4) and thyroid peroxidase antibodies
- Ammonia level
- If neurologic symptoms present, brain imaging and testing for limbic encephalitis

Perhaps the most difficult psychiatric condition to distinguish from PPP is postpartum obsessive-compulsive disorder (OCD). There is evidence of an increased risk of onset and flare of OCD during times of reproductive transition,[57,58] and it is important to distinguish between the frightening intrusive thoughts common in OCD (obsessions) and the delusions that characterize PPP. See **Table 1** for a description of these differences.

In addition to these psychiatric conditions, there are several medical conditions that must be considered in suspected cases of PPD. The waxing and waning of consciousness that is often seen is reminiscent of delirium, and delirium for medical causes (most commonly infection surrounding parturition) should be at the top of any clinician's differential. Tests of attention and cognitive function, such as the Mini-Mental State Examination and the Montreal Cognitive Assessment, can help to determine whether delirium is present, as can laboratory tests, including urinalysis and complete blood count. There have been several cases of autoimmune encephalitis presenting as PPD; postpartum abnormalities, such as Sheehan syndrome or flares of autoimmune diseases (such as lupus), can also have neuropsychiatric presentations.[59] See **Box 7** for a complete differential list.

Table 1
Obsessions versus delusions

Obsessions	Delusions
• Intrusive thoughts that are unwanted and horrifying to patients	• Fixed false belief
• Can be sexual, religious, or violent	• Content often bizarre or unusual; can also be sexual, religious, or violent
• Patient has no desire to act on these thoughts	• Patients may want to act on these thoughts or feel compelled to do so
• Thoughts cause considerable distress and patients may avoid things or engage in compulsive behavior (checking, seeking reassurance) to ease that distress	• Thoughts may not cause significant distress
• *Example: Mother has an intrusive thought about molesting her child while changing diapers; this horrifies her and she insists that her husband change all diapers.*	• *Example: Mother thinks her child has been cursed by the devil and that she must throw him or her out the window.*

Box 7
Differential diagnosis for postpartum psychosis

- Baby blues
- PPD
- Generalized anxiety disorder
- OCD
- Delirium
- Autoimmune encephalitis (ie, N-methyl-d-aspartate receptor)
- Sheehan syndrome
- Autoimmune flare (ie, neuropsychiatric symptoms of lupus)
- Intoxication
- Medication reaction (ie, steroid-induced mania)

MANAGEMENT

Treatment Setting

PPP is a psychiatric emergency that requires inpatient hospitalization. In much of the developed world, that hospitalization can take place in a dedicated mother-baby psychiatric unit, the type of facility that is deemed best practice in many countries.[60] These units, which were first established in the 1950s in the United Kingdom and in the 1970s and 1980s in Europe and Australia, promote mother-baby attachment during the period of treatment of severe mental illness in the postpartum period. Unfortunately, this is a concept that has yet to take hold in the United States, where there are no psychiatric units that permit babies to stay with their mothers. Many clinicians, whether obstetricians or psychiatrists, and many patients and families are, therefore, reluctant to seek hospitalization when it means a disruption of the mother-child bond and a disruption of breast-feeding. The severity of PPP, however, means that in the US treatment setting such separation is usually warranted. PPP is associated with high rates of both suicide and infanticide,[61] and treatment can occur most safely and rapidly in the context of inpatient hospitalization. Any obstetrician encountering a suspected case of PPP should, therefore, seek immediate psychiatric consultation (if inpatient) or refer patients to the emergency department (if outpatient).

Pharmacologic Treatment

The rarity of PPP, and the ethical difficulty of randomizing postpartum patients experiencing a psychiatric emergency, means that the evidence about treatments relies on data from small observational studies only. A 2011 review identified 10 studies of pharmacologic interventions to prevent PPP and 17 to treat it.[49] Approaches studied included antipsychotics, mood stabilizers, hormones, propranolol, and electroconvulsive therapy (ECT), all in either case reports or small observational studies. Some evidence of efficacy was found for all approaches except hormone therapy. The strongest evidence was found for ECT, for which 3 small studies reported improvement for all women undergoing ECT for PPD.

Since that time, the group of Bergink and colleagues,[62] in the Netherlands, has published numerous larger studies on both the cause and treatment of PPP. In the largest treatment trial to date, this group followed 64 women from admission for PPP through

9 months post partum, following a 3-step treatment algorithm. Step 1 was lorazepam at bedtime for 3 days; 4 out of 64 subjects remitted at this stage. Step 2 was the addition of an antipsychotic (usually haloperidol 2–6 mg daily) on day 4; 12 of the remaining 60 subjects remitted at this stage. Step 3 was the addition of lithium after 2 weeks of nonresponse to steps 1 and 2, to a targeted lithium serum level between 0.8 and 1.2 mmol/L; 47 of the remaining 48 subjects remitted at this stage (with the remaining patient discharged against medical advice before remission). Step 4 was ECT after 12 weeks of nonresponse to steps 1, 2, and 3; no subjects advanced to this stage. The investigators tapered off benzodiazepines and antipsychotics after symptom remission and continued lithium (or antipsychotics if patients responded without lithium) for 9 months, with nearly 80% of patients retaining full remission at 9 months post partum.

This timetable for treatment is unrealistic in US treatment settings, where the average acute psychiatric hospitalization lasts only 10 days.[63] Because 98% of subjects in Bergink and colleague's[62] study responded to lithium, most perinatal psychiatrists recommend the early addition of lithium. Because there is a high rate of recurrence (more than 54% recurrence of PPP in one recent study),[16] prophylaxis with lithium is recommended for subsequent postpartum episodes. This recommendation is based on the treatment algorithm of Bergink and colleagues,[62] as described earlier; in that study, only 10% of those maintained on lithium throughout the follow-up period relapsed. Another study of women maintained on lithium throughout pregnancy found a relapse rate of 11% during pregnancy and 29% in the postpartum period for any mood episode, including PPP.[64] (There has not yet been a study, however, that has examined the efficacy of prophylaxis specifically for subsequent pregnancies in women who have experienced PPP.) Although there are risks to using lithium in both pregnancy and breastfeeding,[65,66] those risks are much lower than was once thought and for many women will be outweighed by the risks of PPP (which include suicide, infanticide, poor mother-child bonding, and subsequent PPD with consequences for child development). See **Box 8** for a recommended treatment algorithm.

Psychosocial Supports

Given the severity of symptoms, pharmacologic treatment is always necessary in PPP. Low socioeconomic status and acute stressors increase women's risk for PPD[11] but do not affect the risk for PPP, and evidence concerning psychosocial treatments is weak. Yet family and other psychosocial support is crucial for recovery in PPP. Regardless of the type of mood symptoms involved (manic, depressive, or both),

Box 8
Treatment recommendations for acute postpartum psychosis

- Benzodiazepine (lorazepam 0.5–1.5 mg 3 times a day)
- Antipsychotic (high potency preferred, haloperidol 2–6 mg or olanzapine 10–15 mg)
- Lithium (to achieve serum level of 0.8–1.2 mmol/L)
- Tapered benzodiazepine and antipsychotic once symptom remission achieved
- Continued lithium monotherapy for 9 months (can lower to achieve serum level of 0.6–0.8 after symptom remission if severe side effects)
- For future pregnancies: prophylactic lithium monotherapy beginning during pregnancy or immediately post partum

insomnia is a prominent feature of the illness; sleep hygiene interventions are crucial. Support for the other parent, if any, is also important, as is specific feedback designed to improve the mother-baby interaction. Some groups have used video feedback, individual interventions by nursing staff, or baby massage.[62,67]

Patient and Child Safety

Perhaps the scariest aspect of PPP for the practicing obstetrician is how to determine whether patients are a danger to themselves or their children. Because rates of suicide and infanticide are high,[61] it is important to assess this and to remember that it is always better to err on the side of extra caution. Women with psychiatric illness can and do make excellent mothers, but those with acute PPP may be in danger of harming their children either deliberately or through neglect in the throes of illness. Involve psychiatry if at all possible in making this determination; it is easy for nonspecialists to misinterpret intrusive, obsessional thoughts for psychotic thoughts.

SUMMARY

PPP is a devastating complication of childbirth that carries high risks for both mother and child. Any suspected case requires a thorough psychiatric evaluation as soon as possible. The rarity of the disorder makes it difficult to study; the amount we do not know about risk factors, prevention, and treatment is large. Nevertheless, there are certain key clinical features and risk factors of which the practicing obstetrician can and should be aware:

- Remember that women with known bipolar disorder are at greatest risk but that only one-third of women who present with PPP will have a prior psychiatric history.
- Remember to ask all patients about their personal and family history of bipolar disorder.
- Remember that primiparous women are at the highest risk.
- Always ask about sleep disturbance: Although all new mothers will have disrupted sleep, those who are not able to sleep when they have the opportunity should raise a red flag.
- Always ask, in a neutral and nonjudgmental way, about the woman's thoughts of harming herself or the child; remember that the important distinction is whether a woman is disturbed or horrified by these thoughts (indicating that they may be obsessions).
- Remember that PPP is a psychiatric emergency; if you suspect it, patients must have a psychiatric evaluation as soon as possible (in the emergency department if necessary).

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