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# Postpartum Psychosis

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**Abstract**

**Purpose of Review** Postpartum psychosis is a psychiatric emergency that can affect the health and life of mothers, infants, and families. Postpartum psychosis (PPP) is distinct from non-postpartum psychosis in many ways, and it is crucial to study and understand PPP to identify, treat, and possibly prevent this condition. We therefore sought to review the latest research findings about PPP with the intention of updating readers about the latest evidence base.

**Recent Findings** Multiple physiologic pathways have been implicated in the development of PPP, and further understanding these pathways may allow for early detection and treatment. Risk assessment and treatment should include consideration of the woman patient but also the mother-infant dyad and the larger family.

**Summary** It is our hope that this review of research updates in postpartum psychosis may inform clinical practice and promote specialized, evidence-based diagnosis, risk assessment, and treatment.

**Keywords** Postpartum psychosis · Postpartum · Psychosis · Bipolar · Recovery · Partners

## Introduction

Postpartum psychosis (PPP) is rare, affecting between 1 and 2 per 1000 women. However, postpartum psychosis can develop rapidly and place the life of mother and infant in danger related to its symptoms which may include delusions, hallucinations, severe mood symptoms, and cognitive symptoms. Jones [1] noted that "childbirth is a potent trigger for severe mood disorder, and this link gives us unrivaled opportunities for research into etiology. In no other scenario can we identify individuals, currently well, who are at such a high risk of experiencing a severe episode of mental illness in a defined two-week period." This article will discuss research updates in the past few years about PPP. We will first review the epidemiology of postpartum psychosis, and then we will explore the symptoms of postpartum psychosis and how these symptoms differ from non-postpartum illness. We will explore new research regarding the etiology of postpartum psychosis. We will then review the risk factors of untreated postpartum psychosis. Finally, we will discuss treatment and recovery from postpartum psychosis.

## Postpartum Psychosis Symptoms

Women with a history of bipolar disorder are at a higher risk of developing PPP. Similarly, after experiencing postpartum psychosis, mothers have a 50 to 80% chance of another psychiatric episode, which is usually within the bipolar spectrum [2]. PPP may be the first presentation of bipolar disorder. DiFlorio and colleagues found that among 887 women with bipolar disorder who had children, previous history of affective psychosis in the perinatal period or depression was the most important predictor of perinatal recurrence and could be useful in individualized risk assessments [3].

Postpartum psychosis often presents differently from other psychoses. Symptoms of PPP may include not only delusions and hallucinations, but also manic and depressive symptoms and cognitive symptoms. PPP delusions evolve more quickly and often center on infants. Dysphoric mania and cognitive symptoms include a delirium-like presentation. These symptoms usually begin suddenly in the first

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few weeks postpartum and often present as a psychiatric emergency [2].

Gordon-Smith and colleagues conducted a within-subjects study and collected detailed information about symptomatology in women with postpartum manic episodes compared to women with non-partum manic episodes [4]. They observed differences in symptoms compared to women with postpartum mania, with PPP specifically demonstrating more depressive symptoms, more perplexity and self-reproach, and fewer classic manic symptoms such as pressured speech and sociability.

Women with PPP may also exhibit prodromal symptoms that may be mistaken for medical illness. Prodromal symptoms may include irritability, mood changes, confusion or disorientation, and insomnia. The differential diagnosis includes infection, thyroid disease, parathyroid disease, substance-related symptoms, blood loss, tumor, autoimmune disorder, or anoxia. Serum and urine laboratory testing is important. Neurological testing such as CSF, MRI, and EEG should be considered [2].

Because the typical onset is 3 to 10 days after birth, a woman may have been discharged from the hospital already, and family may not be aware of the symptoms to monitor for. Screening for PPP is difficult due to the range of presentation, the fluctuation over time, and the hidden nature of the disorder. One idea with some potential is the use of an adapted prodromal questionnaire (PQ-16) [5].

The diagnosis of PPP, though described since the time of Hippocrates [6], is not included in the DSM [6, 7]. Work has been underway to justify its inclusion in future editions [7]. A lack of understanding of PPP may lead to missed diagnoses as well as difficulties in explaining PPP in the courtroom after tragedy [6].

## Epidemiology

Perry et al. reviewed phenomenology, epidemiology, and etiology [8]. They noted that "evidence indicates most episodes to be manifestations of bipolar disorder and a vulnerability to a puerperal trigger." They noted that in many cases, PPP is characterized by mania or a mixed-mood episode; however, extreme confusion, depression, and anxiety are common. Peak timing of onset is from days 1 to 14, with a duration of weeks to months and a prevalence of 1-2 per 1000 [8]. Evidence suggests that homicidal thoughts are more common in PPP, yet infanticide is rare occurring in between 1 and 4.5% of cases. Patients also more frequently report thoughts of self-harm.

Perry et al. further note, "compared to before or during pregnancy, the postpartum period has been demonstrated as a time of particularly high risk of severe psychiatric disorders, implicating childbirth in the triggering of these episodes.… While more than 40% of women affected by postpartum psychosis have no history of severe psychiatric illness, the remainder present with a recurrence of pre-existing psychiatric illness" [8]. Of women with PPP who decide to have more children, more than half are at risk to experience another perinatal mood episode. Regarding obstetric risk factors, they note, "only primiparity has been reliably associated with the onset of PPP" [8]. Taylor et al. considered relapses of serious mental illness—defined as psychotic or bipolar disorders among 452 full-term pregnancies - and found 28% were associated with relapse, defined as acute admission within 3 months postpartum [9]. Another prior recent relapse was an independent predictor of relapse in the postpartum. Therefore, women with a recent history of relapse should be warned regarding the subsequent high risk of relapse.

Among live births in Denmark and Sweden, Warselius et al. found "death of a close relative, one of the most severe sources of stress, before or during pregnancy was not associated with postpartum psychosis. Therefore, these data do not support the hypothesis that severely stressful life events, such as bereavement around the time of pregnancy, are associated with postpartum psychosis [10]."

Perry et al. followed 128 women with bipolar disorder from 12 weeks gestational age through 12 weeks postpartum using semi-structured interviews, questionnaires, and case note reviews [11]. Though focusing on bipolar disorder, they found high rates of perinatal recurrence of symptoms among the women.

One study evaluated the relationship between personality traits and the development of PPP [12]. Perry et al. collected information about various personality metrics in pregnant women with bipolar I disorder and observed differences between women who had a history of PPP versus those without any history of perinatal psychiatric symptoms. They did not observe any difference in personality traits, cognitive styles, or affective temperaments between these two groups.

## Pathophysiology

### Stress

Newer studies have re-affirmed previously known risk factors including genetics, likely contribution of rapidly declining estrogen postpartum, and sleep deprivation [13]. Newer studies have focused research on particular roles of stress. While others [10] did not find an association between stressful events surrounding pregnancy and PPP, there is some suggestion that early childhood stress may have some effect. In a small prospective study comparing those at risk for PPP who developed PPP versus those who did not, women who experienced PPP had more elevated CRP, cortisol, and severe childhood maltreatment [14•]. This same group conducted a larger study that reaffirmed findings regarding elevated mid-day cortisol in 3rd trimester/postpartum and higher rates

of severe childhood maltreatment, although CRP no longer became significant [15•]. Women who were at risk for PPP but did not develop it showed significant elevation in cortisol and rates of childhood maltreatment compared to healthy controls, but not to the extent of women who developed PPP. Of particular note, again, perceived stress during pregnancy did not correlate with a higher risk of PPP.

## Genetics

Another area of interest in research is the relationship between genetics, and specifically genetic risk scores, and the development of postpartum psychiatric illness. Bauer et al. conducted a nested case–control study of women in a Danish population-based register in order to characterize the relationship between genetic risk scores (GRS), a measurement of genetic liability characterized by multiple risk alleles that increase the risk of psychiatric illness and postpartum psychiatric illness [16]. They sought to observe whether a GRS for major depressive disorder, bipolar disorder, and schizophrenia was predictive of postpartum psychiatric illness. Although they observed a relationship between GRS scores for major depressive disorder and schizophrenia with the development of postpartum illness, bipolar disorder GRS was not associated with an increased risk of postpartum illness.

Di Florio et al. conducted a case–control study of women in order to determine whether or not polygenic risk scores (PRS) were implicated in the development of first-onset PPP [17]. They noted that women with first-onset PPP had similar bipolar disorder and schizophrenia PRSs as women who were parous and had a history of bipolar disorder, and both groups had significantly higher risk scores compared to healthy controls. Interestingly, women with first-onset PPP had similar PRSs for major depression as healthy controls.

Genetic variants in folate metabolism are another area of interest in the potential etiology of PPP for several reasons, including a significantly increased need for folate in pregnancy and the association between low folate levels and other psychiatric illnesses. Morris et al. conducted a prospective, longitudinal study evaluating whether a relationship existed between a folate-metabolizing gene (MTHFR C677T) of folate metabolism, folate levels, and psychiatric symptomatology [18]. Their data illustrated that a relationship may exist between folate levels and postpartum illness, but this association varies and may be mediated by certain genotypes of the MTHFR gene. They also noted that high levels of homocysteine, a byproduct of low folate, may be associated with psychiatric postpartum illness.

## Neuroimaging

Another area of interest is changes in brain functioning in PPP. Pregnancy and postpartum are times of dynamic brain growth and change [19]. Many of these changes likely present adaptive benefits for motherhood. However, these changes may also make brains more vulnerable to mental illness.

Two studies used functional neuroimaging to study women at risk of PPP and observed functional differences in these women compared to women not at risk of PPP. Kowalczyk et al. observed that women at risk of PPP, compared to healthy controls, demonstrated functional differences in tests of working memory and emotional recognition [20]. Women were deemed to be at risk of PPP based on multiple factors, including if they had a personal or family history of bipolar disorder, schizoaffective disorder, or PPP [20]. The authors noted that patients with non-postpartum psychosis typically demonstrated reduced connectivity with the dorsolateral prefrontal cortex and other areas of the brain. In contrast, women at risk of PPP demonstrated increased connectivity between the dorsolateral prefrontal cortex between these same areas. Women at risk of PPP also demonstrated differences in functioning in tests of working memory and emotional recognition compared to women not at risk of PPP. Sambataro et al. observed changes in the areas of the brain implicated in executive functioning in women at risk of postpartum psychiatric illness compared to women not at risk of postpartum psychiatric illness [21]. In this study, women were deemed to be at risk if they had a personal history of bipolar disorder, schizoaffective disorder, or PPP [21]. They observed that women at risk of PPP exhibited increased connections between areas involved in executive functioning but decreased connections between these areas when engaging in an emotional task.

## Endocrine

Several studies have examined the relationship between endocrine and immune factors and PPP. The unique role of the COVID-19 pandemic was considered in two case series, one looking at PPP in 3 asymptomatic women with COVID-19 [22] and another considering 9 cases of PPP in their hospital, with 3 having tested positive for COVID-19 and 1 receiving vaccination 3 weeks postpartum and developing PPP 4 weeks postpartum [23]. Neither series could identify COVID-19 as a particular precipitant of PPP, with both noting that a large role likely related to the effect of social isolation, particularly if needing to quarantine postpartum [22, 23].

Steroid hormones may also be implicated in the development of PPP, as evidenced by animal and human studies that observe a relationship between brain functioning and enzymes that process steroids, the steroid substrates, and the products [24, 25].

One study considering neuroactive steroid mechanisms particularly focused on the role of steroid sulfatase (STS) and the ratio of DHEA-S to DHEA in mammal models and correlative human data, given DHEA's role as an estrogen precursor [24]. Some of the early promises for this relate to the steroid sulfate axis exerting disproportionately large effects

during 3rd trimester and postpartum periods, STS deficiency reducing available estrogen and its neuroprotective effects (during an already plummeting milieu of estrogen during postpartum), and some genetic deletions encompassing STS being associated with primary psychotic disorders [24].

Sethy et al. conducted a cross-sectional study evaluating thyroid function in women with PPP compared to women with psychosis without postpartum onset and women without psychosis [26]. They observed that women with PPP had higher right thyroid lobe volume compared to the other two groups and higher FT4 levels compared to healthy controls, which could indicate differences in thyroid function causing these structural differences, and therefore indicating a potential relationship between thyroid structure and function and PPP.

### Immune System and Inflammation

Immune system dysfunction may also be implicated in PPP, although some have noted that it is unclear whether the immune system dysfunction is implicated in the etiology of PPP or rather a sequela of PPP [27]. Dazzan et al. proposed that T cells and their effect on brain myelination may be implicated in PPP [28] based on clinical and animal studies. Therapies that target related proteins may therefore potentially mitigate the likelihood of the development of PPP. de Witte et al. also noted that the immune system has been implicated in the pathogenesis of PPP [29]. They therefore set out to observe whether or not exposure to certain central nervous system pathogens was implicated in the risk of PPP. They compared levels of immunoglobulin G and immunoglobulin M to herpes simplex type 1 (HSV-1), herpes simplex type 2 (HSV-2), Epstein-Barr virus (EBV), cytomegalovirus (CMV), and Toxoplasma gondii (TG) in women with a history of PPP to women without such a history. Differences in antibody levels between these two groups were not observed, suggesting that exposure to these pathogens is not a risk factor for the development of PPP.

## Risk Assessment of Postpartum Psychosis

Risks of inadequately treating PPP include accidents, suicide, homicide, and neglect. PPP is often considered a psychiatric emergency due to the elevated risk of child harm, infanticide, and suicide. Treatment plans (Table 1) include considering suicide and infanticide risk, ruling out medical causes, hospitalization with a safe plan for the infant, psychoeducation of the patient and family, and medication management [2]. After hospital discharge, consideration of notification of Child Protective Services should occur, if appropriate, based on the risk assessment. As well, family meetings, frequent outpatient appointments, close communication, parenting education, and home support should be considered. Immigrant women and others with limited social support may face circumstances making them potentially more vulnerable to mental illness and making management more complex [30]. Finally, the safety of breastfeeding or pumping should be considered.

Suicide and violence risk in postpartum psychosis continue to be studied. Suicide is a leading cause of maternal mortality. PPP is a mental health crisis accounting for 38% of maternal suicides in the UK [31]. A recent cross-sectional study of childbearing women found that suicidal ideation and intentional self–harm in the year prior to or after birth increased over a 12-year period [32]. It is unclear if the findings are related to prevalence or detection.

According to Swedish birth registry data, the first postpartum year was associated with a lower risk of suicide [33]. Suicide victims in the postpartum (as compared to living mothers) more often had psychiatric disorders, affective disorders, and a history of self-harm. (ARR for psychotic disorders 83.69; 95% CI 36.99–189.31).

Primary prevention includes considering the established risk factors, including the history of bipolar disorder or postpartum psychosis. Women with risk factors for PPP should be seen by a psychiatrist during pregnancy and have pre-birth planning meetings, strategies to ensure sleep, and pharmacologic plans. Secondary prevention includes early detection. One must keep in mind that symptoms fluctuate over time and women may or may not report suicidal or infanticidal thoughts. Finally, tertiary prevention includes the management of postpartum psychosis [34].

One area of interest is in possibly predicting the severity of PPP, including those who may require hospitalization, using technology. A machine-learning approach using administrative health data of inpatient live births in Queensland, Australia, has been used to predict hospitalization in

**Table 1** Treatment for postpartum psychosis

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|---|---|
| Hospitalization | PPP is a psychiatric emergency requiring inpatient hospitalization. Mother-baby units, if available, are ideal options to maintain the dyadic relationship when safe. |
| Medications | Lithium remains the first line for prophylaxis and treatment of acute PPP.<br>Antipsychotics and benzodiazepines are helpful as adjunct medications.<br>Safety in breastfeeding should be discussed. |
| ECT | ECT is effective alone or as an augmentation to medication management for refractory cases. |
| Therapy | Importance of therapy for mothers, as well as psychoeducation for mothers and families. |

the 12 months after delivery [35]. In the future, this might help identify patients at risk. Predictive risk modeling was also considered after using electronic health records of pregnant women with serious mental illness diagnoses, finding that positive, disorganized, and manic symptoms in the 2 years prior to pregnancy were associated with elevated relapse risk during pregnancy and the postpartum [36].

## Treatment: Medication and ECT

In some ways, the pharmacologic intervention has not been the subject of many recent investigations. Some of this likely relates to the already-established robust efficacy of lithium in the treatment of PPP, as well as that of adjunctive antipsychotics, benzodiazepines, and electroconvulsive therapy (ECT) [37]. There is no current data on the use of newer antipsychotics (cariprazine, lumateperone, brexpiprazole, pimavanserin) for PPP. Despite advancements in neurosteroid treatments for postpartum depression with brexanolone, no studies have evaluated this medication's potential use in PPP.

Further studies supporting the efficacy of ECT in this population have expanded during the last few years. One study utilized the Swedish National Quality Registry for ECT, with retrospective data suggesting a greater rate of response to ECT for those with PPP than for those receiving ECT outside of the perinatal period [38]. There was a significant correlation suggesting higher severity of PPP portended improved responsiveness to ECT. Rates of rehospitalization at 6 months, 1 year, and 2 years were lower for women with PPP receiving ECT than for those receiving ECT outside of the peripartum [39]. A single case study also demonstrated the benefits of ECT in all three episodes of PPP she experienced, including episodes with and without lithium [40]. While novel mechanisms in pharmacology and neuromodulation may not be emerging, the above studies continue to emphasize the uniquely robust response of PPP to these interventions.

## Mother-Baby Units and Bonding

Given that PPP is usually a psychiatric emergency requiring psychiatric hospitalization, mother-baby units (MBUs) have emerged to focus on safety, psychosocial support, and psychoeducation. While initially formed to ensure safety, data is now emerging for the efficacy of MBUs as an intervention for PPP. Specific nursing interventions on MBUs in order to promote safer dyadic interactions and increase support for partners have shown qualitative benefits [41]. One retrospective study of 25 dyads of mothers with PPP (64% involuntary admissions, 100% receiving second-generation antipsychotics, and 16% of women receiving lithium) and their infants displayed improvement in symptoms for all mothers by the time of discharge, and all were discharged with custody of their infant [42].

Postpartum psychosis can significantly impact mother-baby bonding. Of 91 mothers with postpartum psychosis admitted to an MBU, at admission, 18% had impaired bonding with their infants, and at discharge, 6% still experienced impaired bonding. In comparison, mothers with postpartum depression experienced much larger changes over the course of admission. Promisingly, the "prevalence rate of impaired bonding at discharge in women with a diagnosis of [PPP] could be considered equal to that of the general population" [43].

As with the emergence of MBUs, newer research is focusing not only on the long-term recovery of mothers but also on the dyad and support system. A systematic review found five studies that evaluated the involvement of social services in women with acute PPP versus women with established schizophrenia [13]. In one of the studies, 2/11 (18%) of infants of mothers with PPP were placed in foster care, compared to 12/16 (75%) of infants of mothers with schizophrenia. In that study, negative symptoms in women with PPP predicted foster care placement, while greater social support predicted improved chances of the infant going home with their mother. This latter finding was established across all 5 studies of the systematic review, with less social service involvement for PPP given greater rates of socioeconomic and partner support compared to women with schizophrenia, although a major caveat was noted regarding pre-existing negative biases by clinical staff in evaluating schizophrenia versus acute PPP.

For the longer-term recovery of the dyad, there has not been as much data on PPP specifically as about long-term effects of schizophrenia [13]. While self-reported bonding between infants and mothers with PPP is higher than those with postpartum depression, the positive bonding scores are typically not supported by those assessed by clinical staff ratings. The major predictor of perceived bonding stress was the degree of postpartum symptoms which, given the quick onset of PPP, belies the importance of rapid and aggressive treatment for improved outcomes.

## Recovery

The symptom recovery from and recurrence of PPP has been an area of increasing research. One systematic review found that for 20–50% of women with first-episode PPP, they will only have a vulnerability to psychosis in subsequent postpartum periods [13], and one meta-analysis suggested that ~ 43% of those with first-episode PPP will only have psychiatric symptoms in the peripartum [44•].

One prospective study followed 106 women for 4 years after their first episode of PPP and found ~ 32% had a recurrence of affective or psychotic symptoms outside of the peripartum [45]. Unfortunately, there were no identifiable risk factors that were able to predict who would have recurrence [45].

Mothers with a history of PPP described in semi-structured interviews "feeling overwhelmed, scared and confused" and discussed their lack of knowledge about the risk. Forde also noted "barriers to care included staff shortages, poor continuity of care, problems sharing information due to concerns around confidentiality, perceived lack of compassionate care, and inappropriate hospital provision" [46]. Mothers also "expressed a sadness that they had missed out on the expected joys of parenthood." Externalizing the experience allowed them to reduce self-blame and guilty feelings. Over time, the women demonstrated "more compassion and acceptance towards themselves." Women had distressing memories of their hospital admission, in this study, demonstrating the complexity of recovery and women's changing needs over time. They noted that "in the acute phase, emphasis should be placed on providing a safe and suitable environment, building trust and providing access to perinatal services beyond the acute phase, women need to feel connected, re-establish their relationships and be provided with the opportunity to process their experiences and associated sense of loss." They also noted, "finally, as women seek to integrate their experiences, they may benefit from support to maintain their wellbeing, manage fear of relapse, and plan for their future."

There has also been a greater push from mothers who have experienced PPP to process the often-traumatic narrative of the episode through writing, such as through action on PPP. We personally have a few patients who have found sharing their narratives with others (and the providers) to be particularly therapeutic in reclaiming the experience. There are also some narrative analyses looking structurally at some of these published narratives that suggest there is a strong potential role for advocacy and building resilience [47].

### Pop Culture

In 2016, a very popular British television soap opera, *EastEnders*, had an in-depth storyline about PPP, and researchers studied the effects of increased public awareness on women who had experienced PPP [31]. The storyline was important as PPP is generally not well understood by the general public. Subsequently, website visits to a postpartum charity doubled, with a four-fold increase in registration for email peer support after the storyline indicating additional engagement in service prompted by the show. Semi-structured interviews were conducted with participants who had recovered from PPP. Participants perceived an increase ease of disclosure after the storyline because of "increased self-confidence, relevance and topicality of postpartum psychosis," as well as the safety of discussing their own diagnosis after the portrayal. Roberts et al. noted the "perceived value of increasing public exposure was unanimously shared."

## Impact on Partners

Long-term recovery from postpartum psychosis is complex and can involve not only the mother-infant dyad but also the larger family structure as well. In a systematic review of the literature regarding families' experiences of recovery, the four themes found included "experiencing the unspeakable; loss and disruption; realigning old self and new self; and social context" [48•]. In interviews with 13 women and 8 family members, the three themes found were "seeking safety and containment; recognizing and responding to the psychological impact; and planning for the future" [46]. Early on, the emphasis was on safety, later to process their experiences and plan for the future including pregnancies and fears of future relapse.

Themes emerging from semi-structured interviews of 8 partners included "loss, powerlessness, united vs. individual coping hypothesizing and hindsight, barriers to accessing care and unmet needs, managing multiple roles, and positive changes" [49]. They described loss including from having a child or the couple's relationship separation due to hospitalizations. PPP was described as traumatic by partners, with powerlessness and uncertainty about the eventual outcome. Partners felt excluded and unheard. They needed to educate themselves about PPP and often were not asked about their own needs or support. Healthcare professionals often failed to identify the diagnosis and were perceived to lack empathy as well as consistency. Regarding positive changes, these partners noted increasing empathy and understanding about mental health. Elevated rates of separation do occur after postpartum mental health issues.

## Conclusions

PPP varies considerably from psychosis occurring at other times in terms of risk factors, presentation, treatment, and recovery. Understanding PPP is crucial to its detection, treatment, and prevention. Further research is much needed in this area so that vulnerable women can be identified, ideally proactively, and treated effectively, compassionately, and holistically with an eye on the mother, the dyad, and the family unit.

## Declarations

**Conflict of Interest** The authors declare no competing interests.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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