

Is Postpartum Psychosis Incidence Increasing During the COVID-19 Pandemic?

To the Editor:

Postpartum psychosis (PP) refers to a manic, psychotic, psychotic depressive, or mixed state episode (1,2) generally occurring 3 to 10 days after childbirth (3,4). Symptoms can develop rapidly and include hallucinations, delusions, irritability, mood lability, sleep disturbance, and confusion (5). PP is a psychiatric emergency, and the majority of cases require hospitalization (6) owing to increased risk of suicide and infanticide (2,3). The underlying pathophysiology is poorly understood (2,5), and investigation is limited by low incidence, typically ranging from 0.25 (7,8) to 0.6 (9) cases of first-episode PP per 1000 births. However, certain biological mechanisms are theorized to be involved, especially immune system dysregulation and alterations in proinflammatory cytokines interleukin 1 β (10) and interleukin 8 (11). Other findings suggest that stress response contributes to PP development and may be mediated by immune-hypothalamic-pituitary-adrenal axis dysfunction (12).

The COVID-19 pandemic may be contributing to increasing rates of psychosis in the general population (13–17). Case reports have documented associations between heightened pandemic-related fears and vulnerability to psychosis in the perinatal period (14,18) as well as between PP and COVID-19 viral infection (19). Anecdotally, we noticed an apparent increase in patients presenting to our hospital system with PP. To our knowledge, there have been no epidemiological reports estimating PP prevalence or incidence rates during the pandemic. This study investigates the impact of the pandemic on first-episode PP incidence in a clinical sample. Two cases are presented to illustrate the clinical significance of our findings and demonstrate the need for further research in the field.

Methods

This retrospective cohort study compares first-episode PP incidence from year 1 of the COVID-19 pandemic to years prior using admission data from electronic medical records of a large tertiary-care hospital system. This study was approved by our institutional review board. Informed consent was obtained from participants described in case presentations.

Record Identification

During a 3-year period, February 1, 2018, to January 31, 2021, we identified all women of reproductive age, 16 to 40 years, who were diagnosed with PP and/or those with secondary hospitalizations within 90 days of a psychiatric hospitalization for psychotic or manic symptoms. Prior studies suggest 90 days to be the most appropriate cutoff point when using psychiatric admission as the criterion (3,8). Secondary encounters not related to obstetric delivery were then removed. Review of clinician documentation enabled verification of first-episode PP diagnosis using well-established guidelines (5). Notable

exclusions were active substance use, prior manic or psychotic episodes, bipolar disorder, and potentially contributory medical illness (Figure 1) (5).

Statistical Analysis

Analyses were conducted using SPSS version 27.0 (IBM Corp., Armonk, NY), using Quasi-Poisson regression to account for overdispersion. Year and presence of PP were categorical variables, and the count was the dependent variable. The significance level was set to 0.05, and a one-sided test was performed to test the hypothesis that PP incidence was higher in the COVID-19 cohort. The incidence rate ratio was calculated with a 95% Wald confidence interval with Agresti-Coull adjustment to account for rare events.

Results

During pandemic year 1 (February 1, 2020, to January 31, 2021), there were 6 first-episode PP cases, 3554 live births, and an incidence of 1.68 per 1000 live births (Figure 2). Case characteristics comprised the following: age (20 years, 29 years, 32 years, 34 years, 36 years), parity (5 of 6 were G1P1 [gravida 1, para 1], 1 of 6 was G5P4), comorbidities (4 of 6 with no comorbidities, 1 of 6 with preeclampsia, 1 of 6 with obesity, 1 of 6 with asymptomatic COVID-19 positivity on polymerase chain reaction screen). In the 2 preceding years (February 1, 2018, to January 31, 2020), there were 2 cases, 7129 live births, and an incidence of 0.28 per 1000 live births. This incidence is consistent existing epidemiologic study findings (7–9). Case characteristics comprised the following: age (30 years, 40 years), parity (1 of 2 was G4P1, 1 of 2 was G7P5), comorbidities (1 of 2 with obesity, 1 of 2 with preeclampsia and fibroids). An incidence rate ratio of 4.0 was determined with a 95% CI of 1.21 to 13.3 and a *p* value of .0469.

Cases

Patient A had no prior psychiatric history or known COVID-19 infection and began experiencing profound anxiety related to personal and financial stressors brought on by the pandemic at 20 weeks gestation. She presented 1 week postpartum with paranoia, visual illusions, ideas of reference, thought disorder, poor self-care, and sleep disturbance. She recalled, “I noticed people were crossing their eyes at the hospital and I thought they were trying to hypnotize me and control me. I am noticing small things, small dog hairs or fluff, it almost looks like a snake or a worm. And sometimes I see them everywhere, like small worms or sperm trying to burrow into an egg.”

Patient B had a remote history of depression and no known COVID-19 infection history. During her first trimester, she lost her job owing to the pandemic, with resultant financial insecurity. She presented 4 weeks postpartum with visual-tactile hallucinations of shadows turning into people, snakes, and bugs in her bed, and the sensation that an earthquake was occurring. She had intermittent confusion and memory difficulties, and ongoing ego-dystonic suicidal and infanticidal

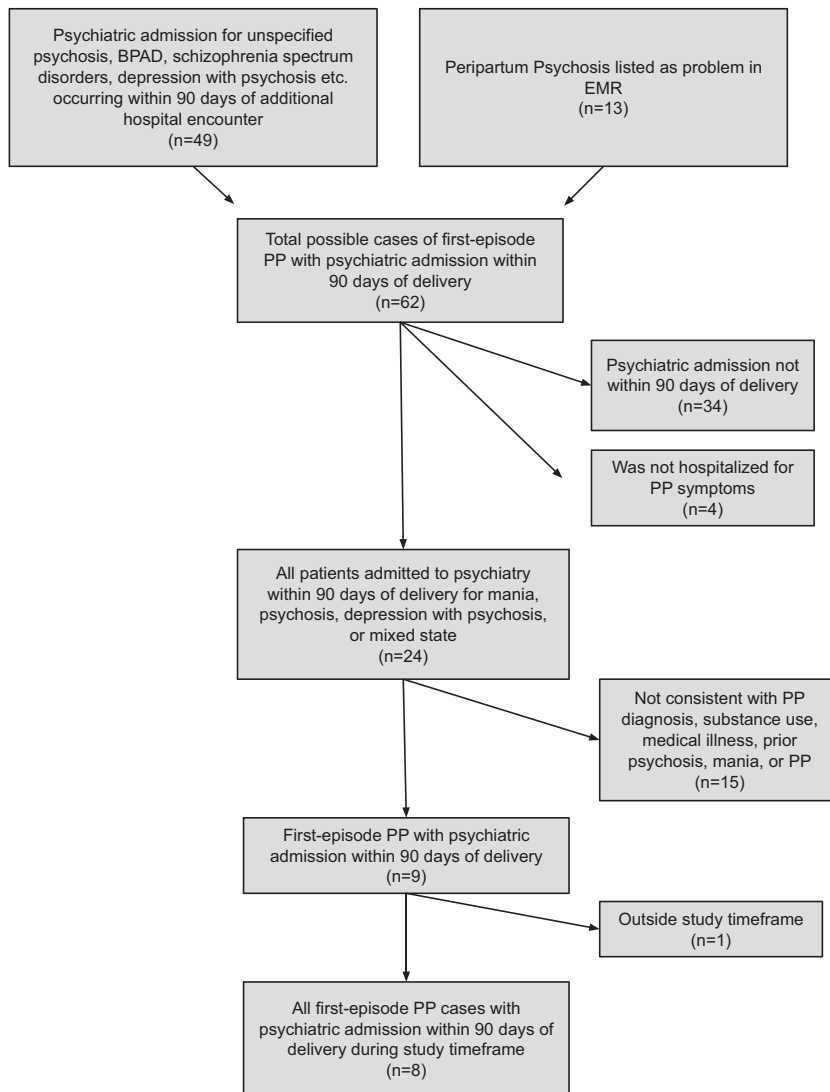


Figure 1. Flowchart of cohort definition methods. BPAD, bipolar affective disorder; EMR, electronic medical record; PP, postpartum psychosis.

ideation, which she experienced as highly distressing and shameful.

Discussion

As our cases demonstrate, PP is a potentially severe condition that can affect those without established psychiatric illness. Historically, incidence tends to be low, yet our findings suggest that rates may have increased during year 1 of the COVID-19 pandemic. This observation exists only within a clinical sample of a single health care institution. Therefore, results are not generalizable to the general public. Nevertheless, these findings have implications for future research involving larger, nationally representative, population-based samples.

Reasons for this apparent rise in cases are likely multifactorial, though there is a strong case for involvement of

pandemic-related psychosocial stressors as illustrated by recent reports (18). Prior work suggests that immune dysregulation may contribute to PP development (10,11), indicating a theoretical basis for subclinical COVID-19 viral infection as an etiologic factor. Even in the absence of infectious process, immune dysfunction is known to contribute to psychopathology during the perinatal period and can be mediated through alterations in stress response and hypothalamic-pituitary-adrenal function (12,20). Further study of the interplay between psychosocial and biologic factors is therefore warranted.

An additional limitation to be noted is that the nature of the pandemic limits our time frame of comparison. COVID-19 may also be affecting rates of hospitalization, theoretically leading to underestimation of PP incidence. Finally, the observations reported in this study do not prove causality and should not change care of pregnant patients. Time and perspective on the

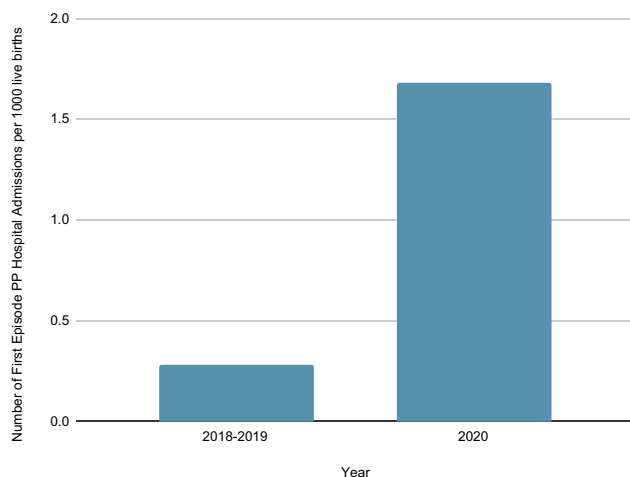


Figure 2. First-episode postpartum psychosis incidence.

pandemic may influence our understanding of these findings, and physicians should remain vigilant in assessing patients for PP as it evolves.

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References

- Bergink V, Lambregtse-van den Berg MP, Koorengavel KM, Kupka R, Kushner SA (2011): First-onset psychosis occurring in the postpartum period: A prospective cohort study. *J Clin Psychiatry* 72:1531–1537.
- Gilden J, Kamperman AM, Munk-Olsen T, Hoogendijk WJ, Kushner SA, Bergink V (2020): Long-term outcomes of postpartum psychosis: A systematic review and meta-analysis. *J Clin Psychiatry* 81:19r12906.
- Kendell RE, Chalmers JC, Platz C (1987): Epidemiology of puerperal psychoses. *Br J Psychiatry* 150:662–673.
- Blackmore ER, Rubinow DR, O'Connor TG, Liu X, Tang W, Craddock N, et al. (2013): Reproductive outcomes and risk of subsequent illness in women diagnosed with postpartum psychosis. *Bipolar Disord* 15:394–404.
- Bergink V, Rasgon N, Wisner KL (2016): Postpartum psychosis: Madness, mania, and melancholia in motherhood. *Am J Psychiatry* 173:1179–1188.
- Perry A, Gordon-Smith K, Webb I, Fone E, Di Florio A, Craddock N, et al. (2019): Postpartum psychosis in bipolar disorder: No evidence of association with personality traits, cognitive style or affective temperaments. *BMC Psychiatry* 19:395.
- Munk-Olsen T, Laursen TM, Pedersen CB, Mors O, Mortensen PB (2006): New parents and mental disorders: A population-based register study. *JAMA* 296:2582–2589.
- Valdimarsdóttir U, Hultman CM, Harlow B, Cnattingius S, Sparén P (2009): Psychotic illness in first-time mothers with no previous psychiatric hospitalizations: A population-based study. *PLoS Med* 6:e13.
- Brockington IF (2014): What is Worth Knowing about "Puerperal Psychosis." Bredenburg, United Kingdom: Ery Press.
- Bergink V, Burgerhout KM, Weigelt K, Pop VJ, de Wit H, Drexhage RC, et al. (2013): Immune system dysregulation in first-onset postpartum psychosis. *Biol Psychiatry* 73:1000–1007.
- Sathyanarayanan G, Thippeswamy H, Mani R, Venkataswamy M, Kumar M, Philip M, et al. (2019): Cytokine alterations in first-onset postpartum psychosis-clues for underlying immune dysregulation. *Asian J Psychiatry* 42:74–78.
- Aas M, Vecchio C, Pauls A, Mehta M, Williams S, Hazelgrove K, et al. (2020): Biological stress response in women at risk of postpartum psychosis: The role of life events and inflammation. *Psychoneuroendocrinology* 113:104558.
- Brown E, Gray R, Monaco SL, O'Donoghue B, Nelson B, Thompson A, et al. (2020): The potential impact of COVID-19 on psychosis: A rapid review of contemporary epidemic and pandemic research. *Schizophr Res* 222:79–87.
- Chandra PS, Shiva L, Nagendrappa S, Ganjekar S, Thippeswamy H (2020): COVID 19 related psychosis as an interface of fears, socio-cultural issues and vulnerability-Case report of two women from India. *Psychiatry Res* 290:113136.
- Rentero D, Juanes A, Losada CP, Alvarez S, Parra A, Santana V, et al. (2020): New-onset psychosis in COVID-19 pandemic: A case series in Madrid. *Psychiatry Res* 290:113097.
- D'Agostino A, D'Angelo S, Giordano B, Cigognini AC, Chitico ML, Redaelli C, et al. (2020): Brief psychotic disorder during the national lockdown in Italy: An emerging clinical phenomenon of the COVID-19 pandemic. *Schizophr Bull* 47:15–22.
- Valdés-Flórido MJ, López-Díaz Á, Palermo-Zeballos FJ, Martínez-Molina I, Martín-Gil VE, Crespo-Facorro B, et al. (2020): Reactive psychoses in the context of the COVID-19 pandemic: Clinical perspectives from a case series. *Rev Psiquiatr Salud Ment (Engl Ed)* 13:90–94.
- Wu Y, Zhang C, Liu H, Duan C, Li C, Fan J, et al. (2020): Perinatal depressive and anxiety symptoms of pregnant women along with COVID-19 outbreak in China. *Am J Obstet Gynecol* 223:240.e1–240.e9.
- Subramanyam AA, Nachane HB, Mahajan NN, Shinde S, Mahale SD, Gajbhiye RK (2020): Postpartum psychosis in mothers with SARS-CoV-2 infection: A case series from India. *Asian J Psychiatr* 54:102406.
- Barch DM, Rogers CE (2019): Maternal depression and child development: Clues to causal mechanisms from potential confounders. *Am J Psychiatry* 176:680–682.