Early and late postpartum depression exhibit distinct correlates: the IGEDEPP prospective cohort study

Sarah Tebeka[1], Yann Le Strat[2], Laurent Mandelbrot[3], Alexandra Benachi[4], Marc Dommergues[5], Gilles Kayem[6], Jacques Lepercq[7], Dominique Luton[8], Yves Ville[1], Nicolas Ramoz[9], Jimmy Mullaert[9], and Caroline Dubertret[10]

[1]Affiliation not available
[2]Hospital Louis-Mourier
[3]Hopital Louis-Mourier
[4]Antoine Beclere Hospital
[5]Assistance Publique - Hopitaux de Paris
[6]Sorbonne Universite
[7]Maternité Port Royal
[8]Hopital Bichat - Claude-Bernard
[9]INSERM
[10]Hôpital Louis-Mourier

June 11, 2020

Abstract

Objective To identify risk factors of early and late postpartum depression (PPD) among a wide range of variables including sociodemographic characteristics, childhood trauma, stressful life events during pregnancy, and history of personal and family psychiatric disorders; and to assess the contribution of each risk factor. Design Nested case-control in a prospective longitudinal cohort study. Setting Eight maternity departments in Paris metropolitan area, France. Sample 3310 women with deliveries between November 2011 and June 2016 Methods Cases were identified as women with early or late PPD. Controls were all cohort participants without either early or late PPD. Main Outcome Measures Early and late PPD are assessed respectively at 2 months and one year postpartum. Results: Stressful life events during pregnancy have a dose response relationship with both early and late PPD: each additional event increased the risk of PPD. In multivariable models, early PPD was independently associated with emotional neglect during childhood (aOR:1.6, 95%CI:1.0-2.6), stressful life event during pregnancy (aOR:1.8, 95%CI:1.4-2.4), physical concomitant chronic disease during pregnancy (aOR:1.5, 95%CI:1.0-2.1), and a history of depression (aOR:1.8, 95%CI:1.4-2.4); whereas late PPD was significantly associated with unemployment (aOR:1.8, 95%CI:1.1-2.8), emotional abuse during childhood (aOR:2.2, 95%CI:1.3-3.9), stressful life event during pregnancy (aOR:2.2, 95%CI:1.6-2.9), emergency consultation during pregnancy (aOR:1.4, 95%CI:1.0-1.8), serious postpartum complications (aOR:1.7; 95%CI:1.0-2.8) and personal and family history of mood disorder (aOR:1.5, 95%CI:1.1-2.0, and aOR:1.4, 95%CI:1.0-1.8). Conclusion: Early and late PPD presented distinct patterns of correlates, with sociodemographic, psychiatric and trauma factors. These results have important consequences in terms of prevention and specific care

Keywords

- Postpartum
- Depression
- Psychiatric history

- Stressful life events
- Childhood trauma

Tweetable abstract:

Early and late postpartum depression are associated with stressful life events and psychiatric history.

INTRODUCTION

Postpartum depression (PPD) is a psychiatric disorder, and one of the main complications of pregnancy, affecting between 10% and 20% of women in the year following delivery (1,2). PPD is a severe disease associated with short-term complications such as suicide, and long-term deleterious consequences, including depressive recurrence (2,3). It may also have negative effects for the child, including disturbances of early interactions (4).

Several types of PPD can be distinguished according to the onset of symptoms, severity and evolution (5–8). Studies over the course of several decades have consistently identified two distinct peaks of PPD: one early in the postpartum period and another later (9–12). Early PPD is usually defined as beginning in the first 6 weeks after delivery, while late PPD develops between the second month and the end of the first year postpartum (13–15).

PPD is a multifactorial disease. Some studies have reported sociodemographic and psychiatric risk factors, including extreme ages, primiparity or grand multiparity (more than 4 children), being single, and personal or familial psychiatric history (1,16–19). The strongest risk factor is a history of mood disorder (uni- or bipolar) (1,20,21). Other psychiatric disorders, such as addictive, anxiety, or personality disorders, are also considered to underlie vulnerability for PPD (17,19,22). Stressful life events are also associated with higher rates of PPD, whether they occur during childhood, adulthood or during pregnancy (1,23). Obstetrical factors, such as unwanted pregnancy, emergency cesarean section, or complications of pregnancy, are also associated with PPD (17,24–26).

While sociodemographic factors, psychiatric history, and stressful events have been individually described to be associated with postpartum depression, their contribution to the specific and independent influence on early or late PPD risk has not yet been characterized. Differences in socio-demographic factors or depression history were found to contribute to the onset timing of perinatal depression (pregnancy or postpartum), establishing different trajectories of depression (9,27). However, to the best of our knowledge, the distinction between early and late PPD has not ever been studied. In addition, very few studies considering PPD have a prospective design, making it extremely difficult to distinguish factors associated with early PPD from those associated with late PPD. While PPD is usually considered as a single disease irrespective of the time of onset of symptoms, our hypothesis is that factors may differ between early and late PPD. Indeed, the emotional and physical state of the mother as well as the environment that she finds herself in change between the first weeks postpartum and several months after birth (28). Mother-infant bonding evolves during the first year postpartum and changes the maternal emotional state; it seems important to determine the differences between these two time periods. A better knowledge of factors associated with early and late PPD is crucial to understanding different physiopathological mechanisms, and to better target women at risk.

We previously reported the prevalence of early and late PPD in a prospective study involving 3310 women evaluated at three times in postpartum, using face-to-face and telephonic interviews, as 8.3% and 12.9% respectively, resulting in one-year cumulative incidence of PPD of 18.1% (29). The aim of the present study is (i) to identify risk factors of early and late PPD among a wide range of variables including sociodemographic characteristics, personal and family history of psychiatric disorders, childhood trauma, and stressful life events during pregnancy, (ii) to assess the contribution of each of these risk factors to the development of early or late PPD.

MATERIALS AND METHODS

Participants

We performed a nested case-control study within the IGEDEPP ("Gene-Environment Interaction in PPD") prospective cohort. IGEDEPP enrolled 3310 Caucasian women in eight maternity departments in the Paris metropolitan area in France, between November 2011 and June 2016. Caucasian cohort participants were selected in order to remove potential confounding factors for genetic analysis. Other main inclusion criteria were: age over 18, and delivery after 32 weeks of amenorrhea. Exclusion criteria included mental retardation, dementia or schizophrenia. Women were included in the study at the maternity department between the second and the fifth day after delivery and were evaluated at three time points by specially trained clinicians, over the course of one year. The first assessment took place at the maternity department between the second and fifth day after delivery in a face-to-face interview; the second at 8 weeks postpartum, by phone; the third at one year postpartum, also by phone. Among the 3310 women, 91.1% (n=3015) were assessed at 8 weeks postpartum, and 71.0 % (n=2351) were assessed at 1 year postpartum. Clinical characteristics of the sample have been described in previous work (29).

The research protocol (ClinicalTrials.gov Identifier: NCT01648816) was approved by the Data Protection and Freedom of Information Commissions and the French Ethics Committee (Ile de France I). All women received oral and written information regarding the study and signed a consent form.

Measures

Diagnosis of early and late PPD

PPD was diagnosed using a semi structured interview (DIGS) (30), according to DSM-5 criteria for a major depressive episode (31). PPD was evaluated at two time points: at 8 weeks postpartum (early PPD), and at one year postpartum (late depression). Early PPD was defined as beginning prior to the 6th week postpartum, and was diagnosed at 8 weeks. Late PPD was defined as beginning between two months and one year postpartum: women were assessed at the one year follow-up for the onset and duration of depressive symptoms over the prior 10 months. Thus, late PPD was assessed retrospectively one year after delivery, and could persist at the time of assessment or not.

For all PPD, the date of onset and the duration of symptoms were collected.

Sociodemographics and childhood trauma at the initial evaluation

Socio-demographic characteristics assessed at the initial evaluation included age, marital status, educational level, professional situation and health insurance status.

Childhood trauma (physical and sexual abuse, severe neglect) were assessed using the Childhood Trauma Questionnaire (CTQ), a validated self-administered questionnaire of 28 questions (32). To determine the presence of abuse/neglect, we used the cut-off scores described by Paquette (33).

Stressful life events during pregnancy, assessed at the initial evaluation

The Paykel scale, a validated questionnaire of 64 questions each with a subjective score of the intensity of the impact, was used to identify stressful events (34). Stressful life events were based on subjective experience, as assessed during the initial evaluation. Events were considered as stressful if they had a negative impact considered "marked" or "severe" by the participant. The Paykel scale was administered three time points: at the maternity department, at 8 weeks and at 1 year postpartum.

The 64 items are organized into 11 categories: work, teaching, wealth, health, bereavement, moving, love relationships, legal issues, family, conjugal and other.

Obstetrical events at the initial evaluation

Obstetrical characteristics were assessed by a questionnaire at the maternity department, covering factors known to be associated with PPD in the literature (see details in (Tebeka et al. (29)). Obstetric data collected during the first evaluation regarded: infertility, use of assisted reproductive technology (ART), the existence of a concomitant chronic physical disease, previous pregnancies, multiple pregnancy, one or more emergency consultation or hospitalization during pregnancy, or a complication of pregnancy such as

threatened preterm labor, gestational hypertension or gestational diabetes. Data on delivery included: type of delivery (vaginal or cesarean, before or during labor), use of obstetric analgesia and presence of perineal trauma ([?] 2-degree perineal tear). Information on prematurity (< 37 weeks of gestation), low birth weight (<2500g), maternal or neonatal transfer to intensive care, postpartum hemorrhage and breastfeeding were also collected.

Obstetrical events with a negative impact considered as "marked" or "severe" by the woman were considered as stressful.

Lifetime psychiatric disorder at the initial evaluation

During the first interview, personal psychiatric history was assessed by a trained clinician using the Diagnostic Interview for Genetic studies (DIGS), a semi-structured interview (30,35), adapted to DSM-5 criteria (31). Lifetime prevalence for mood disorders (including major depressive episode, mania, hypomania), obsessive compulsive disorder (OCD), anxiety disorders (including panic disorder, agoraphobia, social anxiety disorder, specific phobia, social phobia, and generalized anxiety disorder), substance use disorders (SUDs, including tobacco, alcohol, cannabis, cocaine, stimulants, opiates and hallucinogens), eating disorders (anorexia and bulimia) and suicide attempts were assessed.

Family psychiatric history (1^{st} degree relatives) of mood disorder, anxiety disorder, schizophrenia, alcohol and substance use disorders, was also assessed using the Family Informant Schedule and Criteria, a validated questionnaire (FISC) (36).

Statistical Analyses

We performed a nested case-control study from the IGEDEPP cohort. We identified 250 cases of early PPD, defined as meeting DSM-5 criteria for major depressive episode at the 8 week interview. Similarly, there were 235 cases of late PPD, identified at the one-year visit. Categories were mutually exclusive, participants with early PPD were not considered as having late PPD even if they met criteria for PPD at the one-year visit. Women without any form of perinatal depression (i.e. neither during pregnancy nor in the first year postpartum) were used as unmatched controls (N=2726).

Descriptive statistics for binary and categorical variables included sample sizes and percentages for each category and according to the case/control status. Multivariable logistic regressions were conducted to quantify the association between PPD and associated factors at a given time point. Odds-ratios (ORs), adjusted for socio-demographic variables (i.e. age, marital status, education level, and employment), are reported along with their 95% confidence interval (CI) and p-values. The significance threshold was set at .05. Socio-demographic variables and variables with a p-value below 0.2 in the first analysis were included as adjustment factors for the multivariable model, using stepwise variable selection to optimize the Akaike information criterion (AIC). All analysis were performed with R, v3.6.1.

RESULTS

Sociodemographic characteristics and childhood trauma (table 1)

Being single was associated with early PPD (OR=1.9, 95% CI 1.0-3.4, p=.043), whereas being unemployed was associated with late PPD (OR=1.9, 95% CI 1.2-3.0, p=.004). Age and educational level were not associated with early or late PPD.

Childhood trauma was twice as common in women with early and late PPD as in women without perinatal depression (aOR=2.2, 95%CI 1.5-3.2, p<.001 and aOR=2.1, 95%CI 1.4-3.0, p<.001 respectively). Regarding the different types of childhood trauma, sexual abuse and emotional neglect were both associated with early (aOR=2.6, 95%CI 1.4-4.8, p<.002 and aOR=2.2, 95%CI 1.4-3.3, p<.001) and late PPD (aOR=2.5, 95%CI 1.3-4.8, p=.005 and aOR=1.9, 95%CI 1.1-3.0, p<.012), while physical and emotional abuse were associated only with late PPD (aOR=2.8, 95%CI 1.4-5.5, p=.004 and aOR=3.1, 95%CI 1.8-5.3, p<.001).

Stressful life events during pregnancy (table 2)

Having at least one stressful life event during pregnancy was associated with both early and late PPD (aOR=2.0, 95%CI 1.5-2.6, p<.001; and aOR=2.3, 95%CI 1.8-3.1, p<.001 respectively). The number of stressful life events during pregnancy was also associated with an increased risk of both early PPD (aOR=1.4, 95%CI = 1.3-1.6 per additional life event) and late PPD (aOR=1.2, 95%CI = 1.2-1.3 per additional life event, p<.001 for both).

Regarding stressful obstetrical events, early PPD was associated with concomitant chronic physical disease, emergency consultation during pregnancy and perineal trauma (aOR=1.6, 95%CI 1.1-1.2, p=.006, aOR=1.3, 95%CI 1.0-1.7, p=.03 and aOR=1.5, 95%CI 1.0-2.3, p=.03 respectively), while late PPD was associated only with emergency consultation during pregnancy (aOR=1.5, 95%CI 1.2-2.0, p=.002). Other stressful obstetrical events were not associated with either early or late PPD.

Personal and family lifetime psychiatric history (table 3)

A history of any psychiatric disorder was significantly associated with early PPD (aOR=2.1, 95%CI 1.6-2.8, p<.001) and late PPD (aOR=1.6, 95%CI 1.2-2.1, p<.001). Histories of depression and suicide attempt increased the risk twofold for both early and late PPD (depression: aOR=2.1, 95%CI 1.6-2.7 and aOR=1.7, 95%CI 1.3-2.3 respectively, p<.001 for both; suicide attempt: aOR=2.1, 95%CI 1.2-3.8 p=.015 for early PPD, aOR=2.4, 95%CI 1.3-4.4 p=.006 for late PPD). History of any anxiety disorders (specific phobia, agoraphobia, social anxiety, generalized anxiety disorder or panic disorder) was associated with an increased risk of both early and late PPD (aOR=1.7, 95%CI 1.2-2.3 p=.002, aOR=1.6, 95%CI 1.1-2.2 p=.007). A history of substance use disorders was significantly associated with higher risk of both forms of PPD (aOR=1.6, 95%CI 1.1-2.5, p=.016 for early PPD and aOR=1.6, 95%CI 1.0-2.4, p=.035 for late PPD), whereas tobacco dependence was more common for those with early PPD than for controls (aOR=1.7, 95%CI 1.1-2.6, p=.015). Eating disorders and alcohol use disorder were not significantly associated with PPD.

A family history of psychiatric disorder was associated with a higher risk of late PPD (aOR=1.5, 95%CI 1.1-2.1, p=.048), but not with early PPD. Women with late PPD were significantly more likely to report specifically familial history of mood (aOR=1.6, 95%CI 1.2-2.1, p<.001) and anxiety disorder (aOR=1.5, 95%CI 1.1-2.0, p=.012) than controls.

Stepwise regression model (table 4)

After variable selection (socio-demographic variables and variables with a P-value below 0.2 in the first analysis), early and late PPD have different explicative models. Thus, early PPD was significantly associated with a personal history of depression, emotional neglect in childhood, stressful life events during pregnancy as well as obstetric factors, and a concomitant chronic physical disease during pregnancy. While factors significantly associated with late PPD included: being unemployed, having a family history of mood disorder, a personal history of depression, emotional abuse in childhood, stressful life events during pregnancy, emergency consultations during pregnancy and postnatal complications (postpartum hemorrhage or ICU stay for the mother).

DISCUSSION

Main Findings

This large prospective study aimed to determine and distinguish the main determinants of early and late PPD. While both forms shared some common factors, several factors were specific to only one form of PPD. Another important finding is that PPD is not only associated with psychiatric risk factors (personal or family history), but also with childhood trauma and stressful life events occurring during pregnancy and delivery. More specifically, early PPD was associated independently with a personal history of depression, emotional neglect during childhood, stressful life events during pregnancy and concomitant chronic physical disease. Late PPD was associated with unemployment, personal and family history of mood disorder, emotional abuse during childhood, stressful life events during pregnancy, emergency consultation during pregnancy, and serious post-partum complications.

Stressful life events during pregnancy were associated with both early and late PPD in our cohort, in accordance with previous studies (2,37). However, the majority of women experience such stressful life events and most do not develop PPD. In the present study, we took into account the woman's subjective experience for each stressful life event and considered the real impact of each event. We have also revealed a cumulative effect of these life events: each additional event increased the risk of PPD. A cumulative effect of stressful life events in the year before pregnancy has been shown to have an impact on depression during pregnancy (38). This "dose-effect" is important in clinical practice: the risk of PPD increases with each additional stressful event.

The impact of childhood trauma on PPD was controversial: some studies reported this association (44,45), while others did not (46,47). Our study not only confirms that childhood trauma is associated with PPD, but also shows that emotional neglect specifically has an impact on early PPD, while emotional abuse is associated with late PPD. Further research is needed to better understand this point.

As with early adversities, we have shown that recent stressful events are also associated with PPD. Regarding obstetric factors before pregnancy, only a concomitant chronic physical disease was associated with early PPD. Infertility and assisted reproductive technology were not associated with PPD, confirming recent findings (39,40). During pregnancy, we highlighted that consulting in the emergency room is an important factor associated with PPD. An Australian study found consistent results, with more emergency room visits during pregnancy among women requiring hospitalization for PPD (41). Whether this is due to an underlying psychological condition, social stress factors, pregnancy complications, or to the stress associated with the emergency consultation itself is not known and needs further exploration. Finally, perineal trauma had an impact only on early PPD, and this effect disappeared with distance from childbirth; confirming the results of Dunn et al. (42). In our study, episiotomy or cesarean section were not associated with PPD. Data on C-section are conflicting (17,43,44).

Having a personal history of a psychiatric disorder was associated with a higher risk of both early and late PPD, which is consistent with the literature (17). One of the most strongly associated factors was a personal history of depression, in line with published data (1,2,17,48). Having a history of anxiety disorder was also associated with early and late PPD although the final model did not retain it, as shown by previous literature (19,49,50). In addition, a history of attempted suicide increased the risk of early and late PPD in our study. In a U.S. population study, a history of attempted suicide was associated with perinatal depression with an adjusted OR of 3.79 (37).

Women with early and late PPD were both more likely to report a family history of mood disorder than controls (53% and 60% vs. 47% respectively). There was a significant difference between women with late PDD and controls for family history of mood disorder disorders ($p<.001$), but not between women with early PPD and controls, suggesting a smaller effect of family history on early PPD. A recent study based on Danish population-based registers found that parental psychiatric history of depression, bipolar disorder or schizophrenia was associated with postpartum psychiatric disorders, especially among women with personal psychiatric history (51). For women with a psychiatric history, the postpartum period appears to be a time frame of vulnerability for depression, suggesting that genetic factors may play a role in PPD.

Strengths and Limitations

The principal strengths of the present study are the prospective, multicenter design and the size of the sample. To the best of our knowledge, this is the largest sample to date to examine the determinants of PPD prospectively, with a good overall response rate at 1 year. In addition, all psychiatric diagnoses are based on a rigorous clinical assessment using DSM-5- criteria. Moreover, the evaluations at 8 weeks and then at 1 year postpartum make it possible to distinguish 2 types of PPD, with different determinants for early and late PPD. Finally, IGEDEPP provides an extensive assessment of a wide range of determinants, including socio-demographic characteristics, personal and family history of psychiatric disorders, childhood trauma, as well as stressful life events during pregnancy and postpartum, whether related to pregnancy or not.

A main limitation of the study is the fact that all included women were Caucasian, due to the original

objective of the cohort: studying genetic determinants of PPD. The women included also had a high level of education and favorable socio-economic conditions. However, the prevalence of postpartum depression as well as prevalence of the psychiatric disorders assessed were consistent with other samples of women, as discussed elsewhere (29).

Interpretation

In order to better understand PPD and to develop targeted prevention practices, several studies have attempted to define subtypes of PPD according to the time of onset, severity or predominant symptoms (5–8). In this study, we chose to distinguish PPD according to the onset of symptoms. Early and late PPD share some common pre-disposing factors: namely a personal history of depressive disorder and stressful life events during pregnancy. However, the two trajectories can also be distinguished: by socio-economic correlates, life events, and associated psychiatric disorders.

Conclusions

This large, prospective, multicenter study highlights risk factors for PPD: a personal vulnerability, in addition to psychiatric history, and environmental factors, as well as childhood trauma and stressful life events during pregnancy. Moreover, we have distinguished different patterns of correlates for early depression and late PPD. Early PPD was particularly associated with a physical chronic disease, while late depression was associated with unemployment, as well as obstetric factors like emergency consultation. Thus, the screening of both mental and physical health during pregnancy is essential in order to offer targeted prevention interventions.

Our results had direct and important clinical implications. Indeed, prevention through earlier identification of at-risk women is the most important strategy in decreasing PPD incidence (52,53). Clinicians should keep in mind that one emergency consultation during pregnancy could lead to an increased risk of PPD.

Whether personal biological vulnerability and stressful life events act independently or interact with one another should be the focus of further studies. With regard to the IGEDEPP cohort, genetic data will be available and will be particularly relevant to the discussion of the genetic aspects of PPD and potentially propose a gene-environment interaction etiology.

REFERENCES

1. Tebeka S, Le Strat Y, Dubertret C. Developmental trajectories of pregnant and postpartum depression in an epidemiologic survey. J Affect Disord. 2016;

2. Howard LM, Molyneaux E, Dennis C-L, Rochat T, Stein A, Milgrom J. Non-psychotic mental disorders in the perinatal period. Lancet. 15 nov 2014;384(9956):1775-88.

3. Metz TD, Rovner P, Hoffman MC, Allshouse AA, Beckwith KM, Binswanger IA. Maternal Deaths From Suicide and Overdose in Colorado, 2004-2012. Obstet Gynecol. 2016;128(6):1233-40.

4. Netsi E, Pearson RM, Murray L, Cooper P, Craske MG, Stein A. Association of Persistent and Severe Postnatal Depression With Child Outcomes. JAMA Psychiatry. 01 2018;75(3):247-53.

5. Putnam KT, Wilcox M, Robertson-Blackmore E, Sharkey K, Bergink V, Munk-Olsen T, et al. Clinical phenotypes of perinatal depression and time of symptom onset: analysis of data from an international consortium. Lancet Psychiatry. juin 2017;4(6):477-85.

6. Baron E, Bass J, Murray SM, Schneider M, Lund C. A systematic review of growth curve mixture modelling literature investigating trajectories of perinatal depressive symptoms and associated risk factors. J Affect Disord. 1 déc 2017;223:194-208.

7. Santos H, Tan X, Salomon R. Heterogeneity in perinatal depression: how far have we come? A systematic review. Arch Womens Ment Health. 2017;20(1):11-23.

8. Fisher SD, Sit DK, Yang A, Ciolino JD, Gollan JK, Wisner KL. Four maternal characteristics determine the 12-month course of chronic severe postpartum depressive symptoms. Depress Anxiety. 2019;36(4):375-83.

9. Stowe ZN, Hostetter AL, Newport DJ. The onset of postpartum depression: Implications for clinical screening in obstetrical and primary care. Am J Obstet Gynecol. 1 fevr 2005;192(2):522-6.

10. Kothari C, Wiley J, Moe A, Liepman MR, Tareen RS, Curtis A. Maternal depression is not just a problem early on. Public Health. aout 2016;137:154-61.

11. Wikman A, Axfors C, Iliadis SI, Cox J, Fransson E, Skalkidou A. Characteristics of women with different perinatal depression trajectories. J Neurosci Res. 5 fevr 2019;

12. Rosenwald GC, Stonehill MW. Early and late postpartum illnesses. Psychosom Med. avr 1972;34(2):129-37.

13. Norhayati MN, Hazlina NHN, Asrenee AR, Emilin WMAW. Magnitude and risk factors for postpartum symptoms: a literature review. J Affect Disord. 1 avr 2015;175:34-52.

14. PACT Consortium. Heterogeneity of postpartum depression: a latent class analysis. Lancet Psychiatry. janv 2015;2(1):59-67.

15. The International Marce Society. The International Marce Society for Perinatal Mental Health. 2015; Disponible sur: http://marcesociety.com/

16. Muraca GM, Joseph KS. The association between maternal age and depression. J Obstet Gynaecol Can JOGC J Obstetrique Gynecologie Can JOGC. sept 2014;36(9):803-10.

17. Raisanen S, Lehto SM, Nielsen HS, Gissler M, Kramer MR, Heinonen S. Fear of childbirth predicts postpartum depression: a population-based analysis of 511 422 singleton births in Finland. BMJ Open. 2013;3(11):e004047.

18. Lanes A, Kuk JL, Tamim H. Prevalence and characteristics of Postpartum Depression symptomatology among Canadian women: a cross-sectional study. BMC Public Health. 11 mai 2011;11:302.

19. Le Strat Y, Dubertret C, Le Foll B. Prevalence and correlates of major depressive episode in pregnant and postpartum women in the United States. J Affect Disord. dec 2011;135(1-3):128-38.

20. Sharma V, Khan M, Corpse C, Sharma P. Missed bipolarity and psychiatric comorbidity in women with postpartum depression. Bipolar Disord. sept 2008;10(6):742-7.

21. Maina G, Rosso G, Aguglia A, Bogetto F. Recurrence rates of bipolar disorder during the postpartum period: a study on 276 medication-free Italian women. Arch Womens Ment Health. oct 2014;17(5):367-72.

22. Sit D, Luther J, Buysse D, Dills JL, Eng H, Okun M, et al. Suicidal ideation in depressed postpartum women: Associations with childhood trauma, sleep disturbance and anxiety. J Psychiatr Res. juill 2015;66–67:95-104.

23. Robertson E, Grace S, Wallington T, Stewart DE. Antenatal risk factors for postpartum depression: a synthesis of recent literature. Gen Hosp Psychiatry. aout 2004;26(4):289-95.

24. Gaillard A, Le Strat Y, Mandelbrot L, Keita H, Dubertret C. Predictors of postpartum depression: prospective study of 264 women followed during pregnancy and postpartum. Psychiatry Res. 28 fevr 2014;215(2):341-6.

25. Strapasson MR, Ferreira CF, Ramos JGL. Associations between postpartum depression and hypertensive disorders of pregnancy. Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. dec 2018;143(3):367-73.

26. Mak JKL, Lee AH, Pham NM, Tang L, Pan X-F, Binns CW, et al. Gestational diabetes and postnatal depressive symptoms: A prospective cohort study in Western China. Women Birth J Aust Coll Midwives. 2018;

27. Fisher SD, Wisner KL, Clark CT, Sit DK, Luther JF, Wisniewski S. Factors associated with onset timing, symptoms, and severity of depression identified in the postpartum period. J Affect Disord. oct

2016;203:111-20.

28. Rossen L, Mattick RP, Wilson J, Clare PJ, Burns L, Allsop S, et al. Mother-Infant Bonding and Emotional Availability at 12-Months of Age: The Role of Early Postnatal Bonding, Maternal Substance Use and Mental Health. Matern Child Health J. dec 2019;23(12):1686-98.

29. Tebeka S, Le Strat Y, De Premorel Higgons A, Benachi A, Dommergues M, Kayem G, et al. Prevalence and incidence of postpartum depression, and its environment factors: the IGEDEPP cohort. Press. 2020;

30. Nurnberger JI, Blehar MC, Kaufmann CA, York-Cooler C, Simpson SG, Harkavy-Friedman J, et al. Diagnostic interview for genetic studies. Rationale, unique features, and training. NIMH Genetics Initiative. Arch Gen Psychiatry. nov 1994;51(11):849-59; discussion 863-864.

31. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th edn) (DSM 5). 2013; Disponible sur: http://www.psych.org/practice/dsm/dsm5

32. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. fevr 2003;27(2):169-90.

33. Paquette D, Laporte L, Bigras M, Zoccolillo M. [Validation of the French version of the CTQ and prevalence of the history of maltreatment]. Sante Ment Que. 2004;29(1):201-20.

34. Paykel ES. The Interview for Recent Life Events. Psychol Med. mars 1997;27(2):301-10.

35. Preisig M, Fenton BT, Matthey ML, Berney A, Ferrero F. Diagnostic interview for genetic studies (DIGS): inter-rater and test-retest reliability of the French version. Eur Arch Psychiatry Clin Neurosci. 1999;249(4):174-9.

36. Andreasen NC, Endicott J, Spitzer RL, Winokur G. The family history method using diagnostic criteria. Reliability and validity. Arch Gen Psychiatry. oct 1977;34(10):1229-35.

37. O'Hara MW, McCabe JE. Postpartum depression: current status and future directions. Annu Rev Clin Psychol. 2013;9:379-407.

38. Rubertsson C, Wickberg B, Gustavsson P, Radestad I. Depressive symptoms in early pregnancy, two months and one year postpartum-prevalence and psychosocial risk factors in a national Swedish sample. Arch Womens Ment Health. juin 2005;8(2):97-104.

39. Amirchaghmaghi E, Malekzadeh F, Chehrazi M, Ezabadi Z, Sabeti SH. A Comparison of Postpartum Depression in Mothers Conceived by Assisted Reproductive Technology and Those Naturally Conceived. Int J Fertil Steril. janv 2020;13(4):277-81.

40. Furmli H, Seeto RA, Hewko SL, Dalfen A, Jones CA, Murphy KE, et al. Maternal Mental Health in Assisted and Natural Conception: A Prospective Cohort Study. J Obstet Gynaecol Can JOGC J Obstet Gynecol Can JOGC. nov 2019;41(11):1608-15.

41. Xu F, Sullivan EA, Forero R, Homer CSE. The association of Emergency Department presentations in pregnancy with hospital admissions for postnatal depression (PND): a cohort study based on linked population data. BMC Emerg Med. 23 2017;17(1):12.

42. Dunn AB, Paul S, Ware LZ, Corwin EJ. Perineal Injury During Childbirth Increases Risk of Postpartum Depressive Symptoms and Inflammatory Markers. J Midwifery Womens Health. aout 2015;60(4):428-36.

43. Bahadoran P, Oreizi HR, Safari S. Meta-analysis of the role of delivery mode in postpartum depression (Iran 1997-2011). J Educ Health Promot. 29 nov 2014;3.

44. Guintivano J, Sullivan PF, Stuebe AM, Penders T, Thorp J, Rubinow DR, et al. Adverse life events, psychiatric history, and biological predictors of postpartum depression in an ethnically diverse sample of postpartum women. Psychol Med. 2018;48(7):1190-200.

45. Meltzer-Brody S, Larsen JT, Petersen L, Guintivano J, Florio A Di, Miller WC, et al. Adverse life events increase risk for postpartum psychiatric episodes: A population-based epidemiologic study. Depress Anxiety. 2018;35(2):160-7.

46. De Venter M, Smets J, Raes F, Wouters K, Franck E, Hanssens M, et al. Impact of childhood trauma on postpartum depression: a prospective study. Arch Womens Ment Health. 2015;19(2):337-42.

47. Robertson-Blackmore E, Putnam FW, Rubinow DR, Matthieu M, Hunn JE, Putnam KT, et al. Antecedent trauma exposure and risk of depression in the perinatal period. J Clin Psychiatry. 2013;74(10):e942-8.

48. Rich-Edwards JW, Kleinman K, Abrams A, Harlow BL, McLaughlin TJ, Joffe H, et al. Sociodemographic predictors of antenatal and postpartum depressive symptoms among women in a medical group practice. J Epidemiol Community Health. mars 2006;60(3):221-7.

49. Guintivano J, Sullivan PF, Stuebe AM, Penders T, Thorp J, Rubinow DR, et al. Adverse life events, psychiatric history, and biological predictors of postpartum depression in an ethnically diverse sample of postpartum women. Psychol Med. 27 sept 2017;1-14.

50. Dindo L, Elmore A, O'Hara M, Stuart S. The comorbidity of Axis I disorders in depressed pregnant women. Arch Womens Ment Health. 2017;20(6):757-64.

51. Bauer AE, Liu X, Byrne EM, Sullivan PF, Wray NR, Agerbo E, et al. Genetic risk scores for major psychiatric disorders and the risk of postpartum psychiatric disorders. Transl Psychiatry. 11 nov 2019;9(1):288.

52. U.S. Preventive Services Task Force. Screening for depression in adults: U.S. preventive services task force recommendation statement. Ann Intern Med. 1 dec 2009;151(11):784-92.

53. Siu AL, US Preventive Services Task Force (USPSTF), Bibbins-Domingo K, Grossman DC, Baumann LC, Davidson KW, et al. Screening for Depression in Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 26 janv 2016;315(4):380-7.

Acknowledgments :

We would like to thank all the clinicians involved in this study, especially Emmanuelle Bertin, Cecile Bourneuf, Jeanne Colombe, Laura Couppa, Fanny Georges, Julie Guiot Madhavi, Celine Hebbache, Marie Le Bars, Cindy Parent, and Alix de Premorel who included and followed the participants.

We thank all the women who participated in the study.

Disclosure of interests: The authors report no conflicts of interest.

Authors' contributions:

S. Tebeka drafted the initial manuscript, and approved the final manuscript as submitted.

J. Mullaert carried out the initial analyses, revised the manuscript, and approved the final manuscript as submitted.

C. Dubertret designed the study, revised the manuscript, and approved the final manuscript as submitted.

A. Benachi, M. Dommergues, C. Dubertret, D. Luton, and L. Mandelbrot created and validated the questionnaire on obstetric characteristics.

A. Benachi, M. Dommergues, G Kayem, Y. Le Strat, J. Lepercq, D. Luton, L. Mandelbrot, Y. Ville, and N. Ramoz, revised the manuscript, and approved the final manuscript as submitted.

Details of Ethics Approval: The research protocol (ClinicalTrials.gov Identifier: NCT01648816), including informed consent procedures, was approved by the French Ethics committee (Ile de France I) on March 2011 (reference numbers: AOM10056, NI10018, IGEDEPP, ID-RCB 2010-AO1315-34) and Data Protection and Freedom of Information Commissions.

Funding: The study was funded by a grant from Programme Hospitalier de Recherche Clinique - PHRC 2010 (French Ministry of Health). The sponsor was Assistance Publique – Hopitaux de Paris (Delegation a la Recherche Clinique et a l'Innovation).

Word count: 3789

	Early PPD (N=250)	Late PPD (N=235)	Controls (N=2726)	Early PPD vs Controls	Early PPD vs Controls	Late PPD vs Controls	Late PPD vs Controls
	N (%)	N (%)	N (%)	OR (95%CI)	P	OR (95%CI)	P
Age (years) <25 between 25 and 40 >40	21 (8.4) 214 (85.6) 15 (6.0)	15 (6.4) 207 (88.1) 13 (5.5)	193 (7.1) 2404 (88.2) 129 (4.7)	1.2 (0.7-1.9) 1 (ref) 1.3 (0.7-2.2)	.49	0.9 (0.5-1.5) 1 (ref) 1.2 (0.6-2.0)	.81
Marital status: single	13 (5.2)	6 (2.6)	78 (2.9)	**1.9 (1.0-3.4)**	**.043**	0.9 (0.4-2.1)	.78
Education level : Primary or high school	26 (10.4)	15 (6.4)	207 (7.6)	1.4 (0.9-2.2)	.12	0.8 (0.5-1.4)	.5
Unemployed	21 (8.4)	26 (11.1)	166 (6.1)	1.4 (0.9-2.3)	.15	**1.9 (1.2-3.0)**	**.0035**
Childhood stressful life event (CTQ, N above threshold)				aOR (95%CI)	P	aOR (95%CI)	P
- Emotional abuse	12 (4.9)	18 (7.7)	68 (2.5)	1.9 (1.0-3.5)	.053	**3.1 (1.8-5.3)**	**<.001**
- Physical abuse	9 (3.6)	11 (4.7)	47 (1.8)	1.9 (0.9-3.9)	.09	**2.8 (1.4-5.5)**	**.0037**
- Sexual abuse	14 (5.7)	12 (5.2)	57 (2.1)	**2.6 (1.4-4.8)**	**.0023**	**2.5 (1.3-4.8)**	**.0049**
- Emotional neglect	28 (11.3)	22 (9.4)	139 (5.2)	**2.2 (1.4-3.3)**	**<.001**	**1.9 (1.1-3.0)**	**.012**
- Physical neglect	3 (1.2)	1 (0.4)	21 (0.8)	1.3 (0.4-4.6)	.64	0.5 (0.1-4.1)	.55
- Any trauma	41 (16.6)	35 (15.0)	211 (7.9)	**2.2 (1.5-3.2)**	**<.001**	**2.1 (1.4-3.0)**	**<.001**

Table 1: Association between early post-partum depression and socio-demographic data and childhood trauma (CTQ)

Abbreviations: CTQ, Childhood trauma questionnaire; PPD: postpartum depression

aOR: OR adjusted for age, marital status, education level and employment

		Early PPD N=250	Late PPD N=235	Controls N=2726	Early PPD vs Controls	Early PPD vs Controls	Late PPD vs Controls	Late PPD vs Controls	
		N (%)	N (%)	N (%)	aOR (95%CI)*	*P*	aOR (95%CI)*	*P*	*P*
Stressful events during pregnancy	**Stressful events during pregnancy**	**Stressful events during pregnancy**	**Stressful events during pregnancy**						
At least one stressful event with negative impact during **pregnancy (Paykel scale)**	At least one stressful event with negative impact during **pregnancy (Paykel scale)**	154 (61.6)	153 (65.1)	1208 (44.3)	**2.0 (1.5-2.6)**	**<.001**	**2.3 (1.8-3.1)**	**<.001**	**<.**
Obstetrical events before and during pregnancy	**Obstetrical events before and during pregnancy**	**Obstetrical events before and during pregnancy**	**Obstetrical events before and during pregnancy**						
Infertility	Infertility	39 (15.6)	38 (16.2)	316 (11.6)	1.4 (1.0-2.1)	.064	1.4 (1.0-2.1)	.064	.06
Assisted reproductive technology	Assisted reproductive technology	23 (9.2)	25 (10.6)	217 (8.0)	1.2 (0.7-1.8)	.54	1.3 (0.9-2.1)	0.20	0.2
Physical concomitant chronic disease	Physical concomitant chronic disease	49 (19.6)	37 (15.7)	356 (13.1)	**1.6 (1.1-2.2)**	**.006**	1.2 (0.8-1.7)	0.32	0.3
Primiparity	Primiparity	149 (59.6)	127 (54.0)	1567 (57.5)	1.1 (0.8-1.4)	.49	0.9 (0.7-1.2)	0.38	0.3
Multiple pregnancy	Multiple pregnancy	10 (4.0)	7 (3.0)	86 (3.2)	1.3 (0.6-2.5)	.48	0.9 (0.4-2.0)	0.86	0.8

		Early PPD N=250	Late PPD N=235	Controls N=2726	Early PPD vs Controls	Early PPD vs Controls	Late PPD vs Controls	Late PPD vs Controls	
Emergency consultation during pregnancy	Emergency consultation during pregnancy	134 (53.6)	133 (56.6)	1269 (46.6)	**1.3 (1.0-1.7)**	**.03**	**1.5 (1.2-2.0)**	**.002**	**.00**
Hospitalization during pregnancy	Hospitalization during pregnancy	36 (14.4)	32 (13.6)	350 (12.9)	1.1 (0.8-1.6)	.54	1.1 (0.7-1.6)	.72	.72
	Threatened preterm labor	13 (36.1)	9 (28.1)	111 (31.7)	1.2 (0.6-2.4)	.65	0.9 (0.4-2.0)	.74	.74
	Hypertension during pregnancy	2 (6)	1 (3)	34 (9.7)	0.58 (0.09-2.05)	.47	0.29 (0.02-1.4)	.23	.23
	Gestational diabetes	7 (19)	5 (2)	47 (13.4)	1.6 (0.61-3.87)	.29	1.1 (0.35-2.9)	.84	.84
	Venous thromboembolic event	1 (3)	1 (3)	5 (1.4)	2.1 (0.11-14.08)	.50	1.8 (0.08-13.3)	.64	.64
Delivery events	**Delivery events**	**Delivery events**	**Delivery events**						
C-section delivery	C-section delivery	67 (26.8)	64 (27.2)	660 (24.2)	1.1 (0.8-1.5)	.48	1.2 (0.9-1.6)	.30	.30
No obstetrical analgesia despite intention	No obstetrical analgesia despite intention	40 (88.9)	48 (94.1)	411 (89.3)	0.9 (0.3-2.5)	.86	1.9 (0.6-6.4)	.30	.30
Perineal trauma	Perineal trauma								
None or minor perineal tear	None or minor perineal tear	47 (25.7)	58 (33.9)	665 (32.2)	1 (ref)		1 (ref)		
Episiotomy	Episiotomy	60 (32.8)	54 (31.6)	648 (31.4)	1.4 (0.9-2.1)	.10	0.9 (0.6-1.4)	.77	.77
Perineal trauma ([?] 2-degree perineal tear)	Perineal trauma ([?] 2-degree perineal tear)	76 (41.5)	59 (34.5)	750 (36.4)	**1.5 (1.0-2.3)**	**.028**	0.9 (0.6-1.3)	.51	.51

		Early PPD N=250	Late PPD N=235	Controls N=2726	Early PPD vs Controls	Early PPD vs Controls	Late PPD vs Controls	Late PPD vs Controls	
Newborn related events (preterm, small for gestational age, NICU)	Newborn related events (preterm, small for gestational age, NICU)	28 (11.2)	22 (9.4)	250 (9.2)	1.2 (0.8-1.9)	.34	1.0 (0.7-1.6)	.89	.89
Early maternal postpartum events (hemorrhage, ICU)	Early maternal postpartum events (hemorrhage, ICU)	10 (4.0)	19 (8.1)	144 (5.3)	0.7 (0.4-1.4)	.38	1.6 (0.9-2.6)	.08	.08

Table 2: Association between post-partum depression and stressor events during pregnancy

aOR: OR adjusted for age, marital status, education level, and employment

Abbreviations: NICU, newborn Intensive Care Unit; PPD, postpartum depression; ICU, Intensive care unit.

	Early PPD (N=250)	Late PPD (N=235)	Controls (N=2726)	Early PPD vs Contro
	N (%)	N (%)	N (%)	aOR (95%CI)*
Personal psychiatric history				
Any psychiatric disease	157 (62.8)	133 (56.6)	1199 (44.0)	**2.1 (1.6-2.8)**
Major depressive episode	122 (48.8)	104 (44.3)	846 (31.0)	**2.1 (1.6-2.7)**
Suicide attempt	14 (5.6)	13 (5.5)	69 (2.5)	**2.1 (1.2-3.8)**
Any anxiety disorder	57 (22.8)	52 (22.1)	408 (15.0)	**1.7 (1.2-2.3)**
Any eating disorder	15 (6.0)	11 (4.7)	105 (3.9)	1.6 (0.9-2.8)
Any substance use disorder	31 (12.4)	27 (11.5)	206 (7.6)	**1.6 (1.1-2.5)**
Tobacco dependence	27 (10.8)	21 (8.9)	173 (6.4)	**1.7 (1.1-2.6)**
Alcohol use disorder	2 (0.8)	3 (1.3)	14 (0.5)	1.4 (0.3-6.1)
Cannabis use disorder	6 (2.4)	7 (3.0)	36 (1.3)	1.7 (0.7-4.1)
Family psychiatric history				
Any psychiatric disorder	169 (67.6)	171 (72.8)	1727 (63.4)	1.2 (0.9-1.6)
Mood disorder	132 (52.8)	140 (59.6)	1287 (47.2)	1.3 (1.0-1.6)
Anxiety disorder	54 (21.6)	64 (27.2)	541 (19.8)	1.1 (0.8-1.5)
Schizophrenia	3 (1.2)	2 (0.9)	42 (1.5)	0.8 (0.2-2.5)
Alcohol dependence or abuse	41 (16.4)	45 (19.1)	395 (14.5)	1.1 (0.8-1.6)
Other substance use disorder	48 (19.2)	51 (21.7)	528 (19.4)	1.0 (0.7-1.4)

Table 3: Association between post-partum depression and personal and family psychiatric history

aOR: OR adjusted for age, marital status, education level and employment

PPD: postpartum depression.

	Early PPD vs Controls	Early PPD vs Controls	Late P
	aOR (95%CI)	*P*	aOR (
Stressor event with negative impact during pregnancy (Paykel)	**1.8 (1.4-2.4)**	**<.001**	**2.2 (1**
Personal history of major depressive episode	**1.8 (1.4-2.4)**	**<.001**	**1.5 (1**
Emotional neglect (CTQ)	**1.6 (1.0-2.6)**	**.03**	
Physical concomitant chronic disease	**1.5 (1.0-2.1)**	**.03**	
Unemployed			**1.8 (1**
Emotional abuse (CTQ)			**2.2 (1**
Emergency consultation during pregnancy			**1.4 (1**
Maternal early postpartum events (hemorrhage, ICU)			**1.7 (1**
Family history of mood disorder			**1.4 (1**
Infertility	1.3 (0.9-1.9)	.15	1.4 (1.
Sexual abuse (CTQ)	1.8 (0.9-3.4)	.07	
Personal history of any anxiety disorder	1.3 (0.9-1.8)	.10	
Personal history of tobacco dependence	1.5 (1.0-2.4)	.06	
Personal history of cannabis use disorder			2.1 (0.

Table 4: Multivariable models for early and late postpartum depression

Abbreviations: aOR, adjusted odds-ratio; CTQ, Childhood trauma questionnaire; PPD, postpartum depression.