

Preterm birth and postpartum depression: interactions with psychosocial stressors and genetic vulnerability.

ABSTRACT

Postpartum depression (PPD) is one of the most common morbidities in the peripartum period with potential harmful effects on mothers, infants and families. Mothers of preterm infants are likely to be more vulnerable to PPD, but robust evidence is currently lacking, as some divergent results and significant methodological limitations have been reported. We aimed at investigating the association between preterm birth (PTB) and PPD, considering the role of sociodemographic variables, psychosocial stressors and genetic vulnerability, by conducting three complementary investigations. **a) Systematic review and meta-analysis:** we aimed to critically analyze studies assessing PTB as a risk factor for PPD over ten years (2008-2018) (n=26). PubMed/Medline, Web of Science and PsycInfo databases were searched. Most of the studies, but not all, supported an association between PTB and PPD. The meta-analysis provided some evidence of higher risk for PPD among mothers of preterm infants assessed after over 6 weeks after childbirth using the Edinburgh Postnatal Depression Scale (EPDS) (OR=1.36, 95% CI 1.04-1.76, I²=24%). However, important limitations included non-adjusted statistical models and great heterogeneity among studies. **b) Cohort study:** We aimed to investigate the association between PTB and PPD, by comparing groups of preterm and full-term mothers living in two Brazilian cities with contrasting sociodemographic indicators (Ribeirão Preto/SP (RP) and São Luís/MA (SL)). A prospective convenience cohort study was conducted, assessing 1,421 women during pregnancy, at childbirth and in the postpartum period. The EPDS was administrated to assess PPD (EDPS ≥12) within six months after delivery. PTB was defined as the delivery before 37 completed weeks of pregnancy. A multivariate Poisson regression was used to estimate relative risk for PPD in both groups. The final analyses models were adjusted for gestational depression, perceived stress during pregnancy, maternal education, family income and maternal self-reported skin color. Frequencies of PPD were not significantly different in mothers of preterm and full-term infants, irrespective of the city evaluated. There was no evidence to support that mothers of preterm infants are at higher risk for PPD after adjustment for confounding (OR=0.60, 95% CI 0.34-1.08 in RP; OR=0.75, 95% CI 0.26-

2.20 in SL). **c) Case-control study:** We assessed the association between PTB and PPD within a year after childbirth and explored the moderation role of psychosocial stressors and genetic vulnerability in a case-control study nested in a cohort (n=843). Conditional logistic regressions and moderation analyses were conducted. Psychosocial stressors included social support, accommodation after delivery, infant's sex and pregnancy planning. Variables related to genetic vulnerability included variants of the serotonin transporter-linked promoter region (5-HTTLPR) and the corticotropin-releasing hormone receptor 1 (CRHR1). Frequencies of PTB were similar ($p=0.69$) in depressed (8.9%) and euthymic mothers (8.0%). However, in the moderating analyses adjusted for confounders, the only interaction term that remained statistically significant was that between PTB and social support (OR = 0.73, 95% CI 0.59-0.91), suggesting the moderation role of social support in the association between PTB and PPD. Enhancing formal and informal social support for mothers of preterm infants might contribute to decrease rates of PPD in this group.

Keywords: Postpartum depression; preterm birth; perinatal mental health; genetic vulnerability; psychosocial stressors.