EDITOR'S CHOICE ARTICLE

HORMONAL CONTRACEPTIVES AND EMOTIONS

Lana Paulić
University of Zagreb, School of Medicine

0009-0007-5646-6271

While the risks of hormonal contraceptives on the cardiovascular system and cancer development have long been recognized, focus has recently turned to their effects on mood changes and mental health in women. Motivated by this, Søren Vinther Larsen, Anders Pretzmann Mikkelsen, Øjvind Lidegaard, and their colleagues from Copenhagen University Hospital, Denmark, explored whether hormonal contraception (HC)-related depression increased the risk of postpartum depression (PPD), compared to prior depression not associated with HC use.

This intriguing cohort study used data from Danish health registers and included women born after 1978 who gave birth for the first time between 1996 and 2017. To ensure clear results, the study excluded women who had never used HC, those who had experienced a depressive episode before 1996, and women with multiple births or stillbirths as well as those with a depressive episode within 12 months prior to delivery. The focus was on depressive episodes linked to HC use, defined as the initiation of antidepressant treatment or receiving a depression discharge diagnosis from an inpatient or outpatient psychiatric clinic within 6 months of starting HC, with PPD as the outcome. Logistic regression analyzed odds ratios for three groups: HC-associated depression, non-HC-associated depression, and no depression. The study included 188,648 first-time mothers, with 84% having used HC prior to their first childbirth. The results revealed that women with a history of HC-related depression were at a statistically greater risk (42%, or rather 32% higher, after controlling for confounding variables) of developing postpartum depression compared to those whose depression was not linked to HC use. Sensitivity analyses confirmed these findings, and when perinatal depression was taken into account, the risk remained elevated, highlighting a significant connection between HC-related depression and a higher likelihood of PPD.

This population-based cohort study found that there is a subgroup of women sensitive to hormonal changes, showing an association between depression linked to HC use and an increased risk of depression during pregnancy and postpartum. The findings suggest that both pregnancy (with high hormone levels) and the postnatal period (with a sharp hormone decline) contribute to depressive episodes in women sensitive to hormonal changes. The study aligns with previous research on the link between HC use and PPD and suggests that hormonal transitions, especially involving estrogen, play a key role in triggering depressive symptoms.

The study's strengths include using national health registers to gather extensive data on a large population over 23 years, minimizing recall bias. However, it is not without its limitations—particularly the inability to confirm whether HC use directly triggered depression in individuals, and the reliance on antidepressant prescriptions or diagnoses to capture only the more severe cases of depression. While potential misclassification bias and challenges in defining new depressive episodes were noted, the sensitivity analyses still provided consistent results, reinforcing the study's overall findings.

The findings suggest that women with a history of depression linked to HC may face a higher risk of PPD, highlighting the potential role of HC-associated depression in assessing PPD risk. It also offers valuable insights for enhancing clinical risk stratification and improving PPD prediction models, paving the way for more tailored reproductive care and treatments focused on hormonal factors in depression. Future research should examine whether these findings apply to other hormonal transitions, such as perimenopause.

REFERENCES:

1. Larsen SV, Mikkelsen AP, Lidegaard Ø, Frokjaer VG. Depression associated with hormonal contraceptive use as a risk indicator for postpartum depression. *JAMA Psychiatry.* 2023;80(7):682-689. doi:10.1001/jamapsychiatry.2023.0807.