Does PTSD during pregnancy increase the likelihood of preterm birth?

Yes—by fourfold. But the risk is among those with both posttraumatic stress disorder and major depressive episode during pregnancy and is independent of pharmacotherapies for these two conditions, according to this prospective study involving more than 2,600 women.

Yonkers KA, Smith MV, Forray A, et al. Pregnant women with posttraumatic stress disorder and risk of preterm birth. JAMA Psychiatry. 2014;71(8):897–904.

EXPERT COMMENTARY

›› **Leena P. Mittal, MD,** Director, Reproductive Psychiatry Consultation Service, Brigham and Women's Hospital, Boston, Massachusetts, and Psychiatry Instructor, Harvard Medical School, Boston.

FAST TRACK

Women with symptoms of both PTSD and major depression during pregnancy had a risk of preterm birth nearly as high as the risk conferred by a previous preterm birth

The decision about whether to treat any mental health condition during pregnancy is complex, and this study adds to the growing body of knowledge that will inform clinicians and patients about the risks associated with the symptoms of mental health conditions such as posttraumatic stress disorder (PTSD), major depression, and anxiety.

Psychosocial stress during pregnancy has been associated with preterm delivery, possibly related to activation of the hypothalamic-pituitary-adrenal axis, which can result in elevations in maternal glucocorticoids and corticotropin-releasing hormone (CRH). The literature describing the association between stress-related conditions, including PTSD, with preterm birth (PTB), has been inconsistent and limited with regard to power, assessment of the burden of symptoms, and confounding variables including psychiatric comorbidity and psychotropic medications that also have been linked with PTB. Disentangling the risks for PTB associated with psychiatric illness from those associated with psychotropic medication will have a significant impact on decision-making regarding the treatment of psychiatric illness during pregnancy.

In this study, investigators sought to determine whether a likely diagnosis of PTSD or use of antidepressants or benzodiazepines during pregnancy is associated with the risk of PTB.

The author reports no financial relationships relevant to this article.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

The presence of untreated or unremitting psychiatric symptoms must be viewed as an exposure during pregnancy, along with consideration of the risks associated with treatment for psychiatric conditions. This study adds to the growing body of knowledge that untreated symptoms of anxiety and mood disorders, in this case likely PTSD and likely major depression, during pregnancy can have a significant effect on pregnancy outcome.

This study demonstrates that while serotonin reuptake inhibitors and benzodiazepines do increase the risk for PTB, the combination of PTSD symptoms and major depressive symptoms independently increases the risk of PTB—to the same magnitude as a prior history of PTB.

›› **LEENA P. MITTAL, MD**

Details of the trial

A total of 2,654 women from 137 obstetric practices were interviewed prior to 17 weeks of pregnancy and classified as positive or negative for major depressive episode (MDE) in the past 5 years, antidepressant treatment, or PTSD symptoms. Information regarding prior pregnancies as well as medication use (focusing on benzodiazepines and serotonin reuptake inhibitors [SRIs]), smoking, alcohol and drug use, and pregnancy complications was collected.

Recursive partitioning, simple, and multivariable logistic regression analysis was used to analyze the data.

The researchers found that for each point increase on the Modified PTSD Symptom Scale, the risk of PTB increased by 1% to 2%, suggesting that the presence of PTSD symptoms (even if insufficient to fulfill criteria for a PTSD diagnosis) or a history of trauma is linked to PTB. The greatest risk of PTB in women with likely PTSD was found among those who also reported symptoms of MDE. Women with both conditions (n = 51) had a risk of PTB nearly as high as the risk conferred by having had a previous PTB (adjusted odds ratio [OR], 4.08; 95% confidence interval [CI], 1.27–13.15).

The estimated risk of this pattern of psychiatric comorbidity was much larger than that for either benzodiazepine (n = 67) or SRI (n = 291) treatment, although a risk for PTB was associated with each medication (adjusted OR, 1.99; 95% CI, 0.98–4.03 for benzodiazepines and adjusted OR, 1.55; 95% CI, 1.02–2.36 for SRIs).

This study has considerable strengths, not the least of which is its longitudinal prospective design, which allowed for multiple time points of assessment, as well as the large sample size of patients experiencing PTSD symptoms. In addition, the investigators were able to evaluate PTSD symptoms in a dimensional analysis with varying levels of severity, rather than a single time point with a single categorical assessment.

Some limitations include the study's inability to consider the role of anxiety disorders other than PTSD, because of the relatively small numbers of those patients. In addition, the assessment of confounding variables did not include psychotropic agents other than SSRIs and benzodiazepines. Increasingly, medications such as mood stabilizers, anticonvulsants, and second-generation antipsychotics are used for primary or adjunctive treatment of mood and trauma-related disorders during pregnancy, and misuse of prescribed medications like opioids can be associated with maternal and fetal stress through withdrawal. The study's authors also pointed out that they did not measure biomarkers such as CRH to correlate the stress experienced by patients with likely diagnoses of PTSD with the PTB outcomes.