The Other Side of the Risk Equation: Exploring Risks of Untreated Depression and Anxiety in Pregnancy

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There has been a good deal of media attention to the use of psychiatric medications in pregnancy. The focus has been primarily on selective serotonin reuptake inhibitors (SSRIs), our mainstay of treatment for anxiety and depression. The popular press tends to focus on the potential harm to a child exposed to medications in utero; and as prescribing physicians, we may be guilty of the same bias. We are well trained in the practice of articulating the risks and benefits of medication interventions. We appreciate the professional, legal, and ethical obligations of articulating the risks and benefits of the medications we recommend, but such explication of treatment is not sufficient. In order to establish true informed consent, we must educate our patients on the equally meaningful and potentially long-term risks of their untreated mental illness in pregnancy.

Women of child-bearing years are particularly vulnerable to psychiatric illness. Studies of community samples estimate that 10% to 25% of pregnant women suffer clinically significant symptoms of depression.[1–3] The data on the risks of untreated maternal depression and anxiety can be difficult to distill because of differing methodologies: a variety of instruments are used to measure depression, anxiety, and global stress levels; and the measurements are taken at variable times throughout gestation. Notwithstanding the heterogeneity of the studies, however, several meaningful clinical findings emerge. Perinatal psychiatric illness appears to increase the risk of preterm labor,[4–6] temperamental difficulties in the newborn,[7,8] and later-life vulnerability to affective and anxiety disorders in the offspring.[9–11] Other links have been made to preeclampsia,[12] spontaneous abortions,[13,14] and low birth weight.[15–17]

Adverse outcomes may be explained in part by the impact of psychiatric illness on maternal behaviors during pregnancy. Neurovegetative and cognitive symptoms of illness may impair a woman's ability to receive optimal prenatal care. Research shows depressed women are less likely to attend prenatal visits, less likely to take prenatal vitamins, and more likely to smoke and use alcohol and other addictive substances.[18]

Additionally, there may be direct neurophysiologic impact of maternal depression and anxiety on the developing fetus. There is a compelling body of literature demonstrating that anxiety and depression are associated with dysregulation (hyperactivity) of the hypothalamic-pituitary-adrenal (HPA) axis.[19] What is less clear is the extent to which HPA abnormalities in anxious and depressed pregnant women impact a developing fetus and subsequent infant and childhood behaviors. A programming hypothesis of psychiatric illness suggests that prenatal exposure to maternal illness, quite likely mediated through the neurohormonal environment, may predispose the fetus to abnormalities in the development of its own HPA axis with resultant vulnerability to temperamental difficulties and psychiatric illness later in life.[20]

Animal research provides strong support for this hypothesis: when researchers stress pregnant rats and rhesus monkeys, their offspring show enduring abnormalities in behavioral and neuromotor development most likely mediated by enhanced HPA activity upon exposure to novelty and stressors in later life.[21,22]

Additionally, human studies show that neonates of depressed mothers have abnormalities in their biochemical profiles similar to their depressed mothers—with elevated levels of cortisol and epinephrine and reduced levels of dopamine when compared to healthy controls.[23,24] These neonates also show inferior performance on measures of neurobehavioral development. Similarly,

prenatal maternal levels of stress and depression have shown to be predictive of temperamental difficulties (negative affect, adaptability, attention) in infants and toddlers.[7,8]

Extending further into childhood, prenatal maternal anxiety and stress have been linked to emotional and behavioral problems in 4-year-olds and 7-year-olds,[9,10] and individual differences in cortisol levels of 10-year-olds.[25] Taken together, these findings lend support to a psychiatric programming hypothesis in humans.

In conclusion, untreated perinatal psychiatric illness is not a benign condition for mother or child. To make a fully informed decision about care during pregnancy, patients must weigh the risks and benefits of their treatment options against the risks associated with their untreated illness.

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