Prenatal Depression and Infant Health: The Importance of Inadequately Measured, Unmeasured, and Unknown Confounds

Chittaranjan Andrade

ABSTRACT

A recent study found that maternal antenatal depressive symptoms were associated with adverse infant general health outcomes and that gestational age, birth weight, and breastfeeding did not mediate the observed relationship. The authors suggested that antenatal depression can have a harmful effect on infant health through disturbed fetal programming driven by maternal symptoms and behaviors that influence the maternal and hence the fetal internal environment. The authors implied that interventions to diagnose and treat maternal depression can have a protective effect against disturbances in infant health. However, because of the observational nature of the study, cause–effect relationships cannot be conclusively stated. This is especially so because there were many confounds that the authors did not consider. The present article provides examples and explanations of how inadequately measured, unmeasured, and unknown confounds can explain observed relationships between explanatory and outcome variables, thereby negating cause–effect interpretations of study findings. It is important to minimize confounding when conducting observational studies, and this can only be done by comprehensively listing and efficiently measuring potential confounders in advance.

Key words: Antenatal depression, bias, cause–effect relationship, confounding variables, infant health outcomes, observational research

INTRODUCTION

Depression is associated with biological changes that range from disturbances in neuroendocrine regulation to disturbances in sleep and appetite. Depression is also associated with self-injurious changes in behavior; patients may smoke, drink, use illicit substances, disregard advice related to current medical conditions, and attempt deliberate self-harm. Thus, the internal environment of a depressed patient is perturbed by the illness itself and by behaviors related to the illness. During pregnancy, the growth and development of the fetus are influenced by maternal health, maternal behaviors, and the maternal internal environment. It

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is, therefore, reasonable to speculate that depression complicating pregnancy can influence fetal, infant, and child health outcomes, and perhaps outcomes in adult life as well. This, in fact, is a matter that has been considerably researched. One recent investigation was that of Coburn et al.[1]

The study by Coburn et al.[1]
The authors[1] studied 322 low-income Mexican-American mothers and their infants. The mothers were assessed at a mean of 35 weeks of gestation and, again, 12 weeks after birth. At both time points, maternal depressive symptoms, if any, were quantified using the Edinburgh Postpartum Depression Scale (EPDS). At the 12-week assessment, mothers also completed a Baby Health Questionnaire that recorded whether or not eight common health disturbances such as fever, rash, and diarrhea had occurred during infancy.

Regression analyses were conducted to assess the relationship between antenatal depression ratings (EPDS scores) and infant health disturbances. Maternal age and the presence of a romantic partner were included as covariates in the regressions. Education, household income, immigrant status, and the number of other children were not adjusted for in the regressions because they were found to have no influence on infant health disturbances.

Important findings in regression analyses were as follows:
1. Higher antenatal EPDS scores were associated with higher postnatal EPDS scores
2. Higher antenatal and postnatal EPDS scores were independently associated with more infant health disturbances
3. Antenatal EPDS scores did not predict gestational age, birth weight, or breastfeeding, and these three variables did not predict infant health concerns.

Coburn et al.[1] concluded that maternal antenatal depressive symptoms may be associated with adverse infant health outcomes and that gestational age, birth weight, and breastfeeding do not mediate the observed relationship. They suggested the need for interventions for antenatal depression to reduce the potentially harmful effects of antenatal depression on fetal and infant health.

Critical comments
Coburn et al.[1] demonstrated an association between the severity of antenatal depression and the magnitude of infant health concerns at 12 weeks after birth. They suggested that antenatal depression can have a harmful effect on infant health through disturbed fetal programming driven by maternal symptoms and behaviors that influence the maternal and hence fetal internal environment. They implied that interventions to diagnose and treat maternal depression can have a protective effect against infant health concerns.

However, a cause–effect relationship between antenatal depression and infant health cannot be determined from an observational study such as this because inadequately measured, unmeasured, and unknown confounds could have explained both antenatal depression and poor infant health, as the following examples show.

Inadequately measured confounds
The authors[1] recorded the annual household income, but this single variable would not have been able to capture the range of environmental adversities that could have affected maternal and infant health. For example, poor living conditions, poor access to nutritious food, and poor access to quality medical care could have been responsible for both antenatal depression and poor infant health. Thus, environmental adversity is an example of an inadequately measured confound because it is not satisfactorily described by the annual household income, alone.

Unmeasured confounds
Maternal physical illness, maternal use of medications, maternal use of alcohol, cigarettes, and illicit drugs, and other variables could have increased the risk of both maternal depression and poor infant care, with the latter resulting in infant health disturbances. Information related to such variables was not recorded. Thus, these are examples of unmeasured confounds. The failure to record whether the women were receiving antidepressant medication is a particularly important unmeasured confound, given that medication exposure during pregnancy can moderate maternal depression severity and worsen fetal and infant health outcomes through direct effects, or improve these outcomes through attenuation of depression.

Unknown confounds
The infant shares some of its mother’s genes. It is possible that genetic influences that are responsible for maternal depression may also influence infant vulnerability to health disturbances. We do not know what these genetic influences are and so cannot measure them. These would be examples of unknown confounds.

Implications
Although this is a promising study,[1] it merely indicates that the severity of antenatal depression, as measured by the EPDS, is a potential marker for infant general health. There is insufficient evidence to posit a cause–effect relationship between antenatal depression and
infant general health. Whereas it is important to diagnose and treat antenatal depression, it is too early to conclude that doing so will result in improved infant general health outcomes.

Parting notes
If researchers do not efficiently collect data on variables that influence the outcomes that they plan to study, they will not be able to determine whether or not these variables bias their findings. The reader is referred to specific articles that explain the concept of confounding and bias in research.[2-4] The possibility of confounding is an important consideration in observational research, such as studies that examine gestational and infant outcomes after depression or antidepressant exposure during pregnancy.

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Conflicts of interest
There are no conflicts of interest.

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