Untreated psychiatric disorder in pregnancy: Weighing the risks

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ABSTRACT

Though approximately 15 to 29% of pregnant patients have a psychiatric disorder during pregnancy, only about 5 to 14% seek treatment. Untreated mental illness during pregnancy has been associated with poor nutrition, failure to follow prenatal and medical guidelines, and alcohol or other substance misuse. The risks of untreated mental illness during pregnancy must be carefully evaluated along with the risks posed by medications. This review will evaluate consequences of untreated depression, anxiety, schizophrenia, and bipolar disorder in the pregnant patient.

KEYWORDS

untreated, mental illness, pregnancy, outcomes

BACKGROUND

Estimates of psychiatric disorders during pregnancy have ranged from 15% to 29%.[1,2] A recent study utilizing a national survey found the 12 month prevalence of any psychiatric disorder during pregnancy was 25.3%. This study also showed results consistent with previous studies which indicated that pregnant women with psychiatric disorders demonstrated a low rate of seeking and receiving mental health treatment in the past 12 months. This is consistent with a report that pregnant women are less likely than non-pregnant women to receive psychiatric treatment, whether the treatment is at an inpatient or outpatient facility.[3] It has also been indicated that psychiatric symptoms and diagnoses are undetected and underreported in pregnant women receiving care in obstetric clinics.[2] Studies have suggested that only 5% to 14% of women obtained treatment of their psychiatric disorders.[1] Failure of pregnant women to receive psychiatric treatment during pregnancy may suggest that there are significant barriers to mental health care for this population. Several reports have found that psychiatric illness during pregnancy is associated with poor nutrition, failure to follow prenatal and medical guidelines, and alcohol or other substance misuse.[4-7] Although information regarding treatment of psychiatric disorders in pregnancy exists and is reported regularly, there are still many unanswered questions when it comes to understanding whether negative outcomes in the developing fetus, the infant and during childhood development are attributable to the psychiatric illness of the mother or psychotropic medications.

When the topic of treatment of mental illness during pregnancy arises, there is the issue of weighing benefits versus risks. The initial focus is often the risks/teratogenicity of medications for the mental illness. Seldom do patients consider the risk of untreated illness as readily as they consider the impact of medications. Contrary to some reports[6], pregnancy is not protective in mental illness. Pregnancy and the post-partum period may actually be periods of increased vulnerability.[1,4] Many women face increased symptoms during pregnancy. Symptoms of psychiatric disorders during pregnancy may lead to adverse fetal, obstetrical, and neonatal outcomes as well as cause risk to the mother and adverse effects on child development.[1,5,7-13] (Table 1) When discussing treatment options for psychiatric disorders during pregnancy, it is just as important to inform patients of the risks of untreated mental illness as it is to inform them of the teratogenicity of medications that they are taking or may potentially take. Patients must understand that there is not a "risk-free" option for treatment. If the risks are not known on both sides, then the patient cannot make a truly informed decision about treatment.

UNTREATED DEPRESSION/ANXIETY

Many of the studies looking at risks of untreated psychiatric illness during pregnancy have focused on untreated depression/depressive symptoms or combination of untreated depressive symptoms/depression and anxiety. The majority of studies have compared outcomes of women with depression to outcomes of non-depressed women. Very few studies have examined outcomes of depressed and/or anxious women who are not medicated or untreated versus depressed and/or anxious women who are medicated during pregnancy.

One of the most widely published and researched theories is the neurophysiologic impact of maternal anxiety and depressive symptoms on the developing fetus and neonate. Literature shows that anxiety and depression are associated with dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. This dysregulation has been linked to poor birth outcomes and negative effects on the infant and child.[4,6,7,14-18] There is also some evidence that increased prenatal maternal cortisol and norepinephrine levels and lower dopamine and serotonin levels correlate with a similar pattern in the neonates born to these depressed mothers.[16] These studies showed that mothers with these biochemical changes were more likely to have infants with low birth weight/restricted fetal growth and to deliver prematurely (shorter length of gestation). The newborns of the anxious/depressed mothers demonstrated higher depressed symptom scores and less optimal performance on the Brazelton Neonatal Behavior Assessment Scale (motor maturity, autonomic stability and withdrawal).[14,16,18] A fetal programming hypothesis of psychiatric illness suggests that the exposure to the prenatal illness (depression/anxiety) may predispose the child to abnormalities in development of their own HPA axis which leads to increased risk of temperamental difficulties (negative affect, adaptability, attention) and psychiatric illness later in life.[4,17] This theory is thought to be supported by results from Huot and colleagues[15] which suggest that increased cortisol levels in response to a mild stressor at 6 months of age predicted negative affect in infants and toddlers. They concluded that prenatal maternal stress and depression are predictive of temperamental difficulties and enhanced stress responsiveness in infants and toddlers.[15] Table 1 Further support is seen in research which indicates a link between maternal prenatal anxiety and stress and emotional and behavioral problems in four year-olds and seven year-olds that were born to mothers that reported high levels of prenatal anxiety and stress.[15,17] Table 1

Therefore, studies exist which suggest that untreated maternal prenatal depression/anxiety may lead to negative outcomes and increased risk in the mother (negative obstetrical outcomes, postpartum effects and impact on family unit)[7,14] as well as the child from fetus through childhood.

Table 1. Consequences of untreated/unmedicated depression and anxiety

Fetal outcomes	↑Fetal heart rate[14] Decreased fetal growth/ Small for gestational age (weight and length)[6,14,18] ↑Fetal activity (5, 6 and 7 months gestation)[18]
Obstetrical outcomes	Preterm labor/birth[14,18] Low birth weight ↑Risk of epidural analgesia[6] ↑operative deliveries[6] Pre-eclampsia[5,13]
Neonatal outcomes	Lower Apgar scores Small head circumference ↓Vagal tone ↑Cortisol levels ↓Dopamine and serotonin levels Some evidence of ↑ admission to neonatal care unit Negative affect Poor neonatal adaptation ↑Irritability and excessive crying Sleep disturbances
Child development	Negative impact on maternal-infant bonding Sleep disturbances[5] ↑Rates of inattention/hyperactivity (ADHD)[5,17] ↑Rates of emotional difficulties[17] ↑Rates of conduct problems[5,17] Difficulties with affect regulations More fearful and anxious More insecure and disorganized attachment styles
Risk/harm to mother	Poor nutrition Poor self-care Failure to attend prenatal appointments Failure to follow medical and prenatal guidelines Increased use and misuse of substances of abuse and/or alcohol ↑Postpartum depression and other psychiatric illnesses Impact on family members

It is important to note that many of the studies to date have compared untreated prenatal depression to control groups of non-depressed mothers as opposed to comparing untreated/nonmedicated depression to treated/medicated depression. In a recent review of untreated prenatal maternal depression by Davalos,[14] only three of the 14 articles met the criteria for the review and compared unmedicated depressed mothers to medicated depressed mothers. The effects or outcomes were measured in the neonatal/infancy stage. The results from these three trials were equivocal. Suri et al.[19] found no significant differences at birth with regard to birth weight, length of gestation, intensive care admissions or Apgar scores (heart rate, respiratory effort, muscle tone and skin color) between the study groups. The study groups consisted of mothers medicated prenatally with fluoxetine, unmedicated prenatally depressed mothers and a control group of non-depressed mothers. Interestingly, neither the medication nor the untreated depression appeared to impact the offspring.

Oberlander and colleagues[20] found that both neonates exposed to medication and those exposed to untreated depression had lower birth weights, shorter gestation periods and longer hospital stays than controls (neonates of non-depressed mothers).

Dayan and colleagues[21] examined the impact of prenatal depression and anxiety on spontaneous preterm birth. This study also looked at three groups; medicated depressed and anxious, nonmedicated depressed and anxious and non-depressed and non-anxious controls. The principal finding was that women with high depression scores were at greater risk of spontaneous preterm birth. Initially, the analysis was done with all depressed patients. To test the role of psychotropics, the analysis was redone excluding psychotropics users and the association was stronger, thus suggesting that the association between preterm birth and depression is stronger amongst unmedicated depressed women as compared to those on psychotropic medication. Anxiety showed no association with the findings.

UNTREATED SCHIZOPHRENIA AND BIPOLAR DISORDERS

There is a paucity of information regarding bipolar illness and schizophrenia in pregnancy.[1,12] A population-based cohort study by Jablensky et al[9] investigated the incidence of complications during pregnancy, labor and delivery and neonatal characteristics of infants born to mothers with schizophrenia (n=618), bipolar disorder (n=1301) and unipolar major depression (n=1255). These three groups were compared to a control group of women without psychiatric illness (n=3129). The authors conclude that both schizophrenic and affective disorder patients had increased risk of pregnancy, birth, and neonatal complications which included placental abnormalities, antepartum hemorrhages and fetal distress. Women with schizophrenia were significantly more likely to have placental abruption, to have low birth weight infants (infants in the lowest weight/growth population decile) and to have children with cardiovascular congenital anomalies. The severe limitations of this study prevent the drawing of important conclusions from this trial. There was a lack of data on smoking, prescription medications and illicit drug use. Therefore, it cannot be determined if the patients were medicated or non-medicated. Finally, there was a lack of information about severity of disorder. There are other population-based cohort studies with similar results and limitations. A major issue that needs to be addressed in these studies is whether the results seen are attributable to the disease process or are a result of the behaviors which may result from severe mental illness. Authors have hypothesized that lifestyles of women with affective disorders are often characterized by poor diet, lack of exercise, and obesity which may be attributed to socioeconomic disadvantage and lack of adequate social support. It is unknown how much unhealthy lifestyle factors may contribute to risk of adverse pregnancy events but this is a major area of concern and potential research. [9,22]

A population-based cohort study by Boden and colleagues[8] did examine the risks of adverse pregnancy and birth outcomes in pregnant women with bipolar disorder who were treated with mood stabilizers (n=320) or not treated with mood stabilizers (n=554). Mood stabilizers were defined as lithium, antipsychotics or anticonvulsants (lamotrigine, valproate, carbamazepine). These two groups were compared with a control group of pregnant women without bipolar disorder (n=331263). Main outcome measures included preterm birth, mode of labor initiation, gestational diabetes, infants who were born small or large for gestational age, neonatal morbidity and congenital malformations.

The study found that women with bipolar disorder were more often overweight, smokers, and misused alcohol or illicit substances as compared to women without bipolar disorder. Infants born to mothers with bipolar disorder had increased risks of preterm birth whether or not the mother was treated with mood stabilizing medications or untreated. Infants of mothers who were non-medicated also had increased risk of microencephaly (small head

circumference) and neonatal hypoglycemia. Untreated bipolar disorder was associated with infants born small for gestational age for weight length and head circumference. This difference decreased and was non-significant after adjusting for confounders. The authors comment that this is supported by other studies that have shown that bipolar disorder is associated with an increased risk of infants being small for gestational age or similarly having small head circumference. The Jablensky[9] trial found that the head circumference being the lowest tenth percentile had an odds ratio of 1.51 for bipolar disorder subjects versus comparison non-psychiatric subjects. Comparison of trials is complicated by the fact that the other trials did not include information on drug use during pregnancy. It is also suggested that the small head circumference is part of a general fetal growth restriction and in line with being small for gestational age. Because being small for gestational age is a risk factor for hypoglycemia, the authors felt that their findings are supported despite the lack of significant difference after adjusting for confounders.

Similarly, Lee et al.[22] investigated pregnancy outcomes in a population based cohort study in Taiwan. The study looked at the outcomes of low birth weight (LBW), preterm births and small for gestational age (SGA) infants among women with bipolar disorder compared to women with no history of psychiatric illness. They found that pregnant women with bipolar disorder were more likely to have LBW infants (9.8% vs. 5.7%), preterm births (14.2% vs. 6.9%) and SGA infants (22.3% vs. 15.7%) when compared to women with no history of mental illness. The adjusted odds ratios for women with bipolar illness as compared to women without psychiatric illness was 1.66. Odds ratios for preterm births and SGA infants were 2.08 and 1.47 respectively when comparing women with bipolar disorder to non-psychiatric controls. This study had similar limitations to the Jablensky trial in that there was a lack of data on smoking, lack of information on prescription medications or illicit drug use and lack of information about severity of disorder. Absence of information about medication status is a troubling limitation.

CONCLUSION

More research is needed regarding the risks versus benefits of untreated/non-medicated psychiatric illness. Studies in the area of treatment of mental illness during pregnancy have overwhelmingly focused on treatment effects associated with psychotropic medications. Yet, the majority of women with psychiatric illnesses during pregnancy are untreated and not medicated. Clinicians require research and resources to be able to competently counsel patients on the risks and benefits of treatment of psychiatric illness during pregnancy with a goal of assisting the patient in making an informed decision about treatment.

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