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PREGNANCY PLUS

Depression during pregnancy

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Introduction

Depression during pregnancy is common. The case presented here highlights many of the key issues involved in the management of pregnant women with depression, particularly the importance of active treatment.

SCENARIO

Two months after the birth of her second child a 34 year old woman was admitted to a psychiatric inpatient unit for treatment of depression. She was married and worked as a business manager. She had a history of depression dating back to her late teens, which had been untreated until the birth of her first child three years before. At this point her depression had deteriorated into a psychotic state, but she subsequently responded to a combination of antidepressants and antipsychotic drugs. Her second pregnancy was planned, and her medication was discontinued when she conceived. Although her mental state continued to deteriorate as the pregnancy advanced, she was reassured at antenatal consultations that she had a healthy pregnancy and her baby was developing appropriately. She went into spontaneous labour and delivered a healthy baby girl at 35 weeks.

In the subsequent weeks her mental health deteriorated further. She believed that she was a terrible mother and that her baby was doomed to a life of misery. She experienced derogatory auditory hallucinations confirming these beliefs and in this deluded state attempted suicide. She was discovered by her sister and brought to a general hospital, where she was treated for two weeks in the intensive care unit. After a further 10 week admission in a specialist psychiatric unit, during which she was reunited with her baby, she was discharged fully recovered on venlafaxine 225 mg and olanzapine 5 mg a day.

How common is depression during pregnancy?

Rates of depression in women are higher during the childbearing years than at any other time.^{w1} Estimated rates of depression during pregnancy vary from 7-15% in economically developed countries^{1 w2} to 19-25% in poorer countries.^{2 w3} This compares with rates of around of 10% during the postpartum period^{w1} and 7% outside of the perinatal period.^{w4} Rates of relapse in pregnant women with a history of recurrent mood disorder are high, at about 50%.^{3 w5} We do not know, however, whether the high prevalence of antenatal depression results only from rates of relapse or also reflects an increased incidence of depression.

Who is at risk?

Across cultures poverty, lack of education, and sex inequality predispose women to depression in pregnancy.^{2 w3 w6 w7} This is reflected in the high rates seen in low income countries, varying from 19-25% in Pakistan,² Goa,^{w8} and Rio de Janeiro.^{w3} Exposure to domestic violence also increases the risk of developing antenatal depression.^{2 w3 w9} Similar effects of social adversity have been found among women living in relative poverty in Europe and America.^{w6 w7} Women with poor social support, with an unplanned pregnancy, and who are single or adolescent are also more vulnerable to depression during pregnancy.^{w10}

How does pregnancy affect depression?

There are many reasons for the increased prevalence of depression during pregnancy. Most women welcome pregnancy but it is also a major physiological and psychological life event. Women who are coping with other more chronic life stressors may find the additional stress of pregnancy unmanageable. Pregnancy also carries specific demands that individual women may have difficulties with, such as impending motherhood if she has had poor parenting herself or if she has been sexually abused as a child.^{w9}

The biological changes during pregnancy also have a direct effect on mood state. Concentrations of female specific sex steroids are raised during gestation and modify parts of the brain involved in mood regulation.^{w11} There are also gradual increases in hormone concentrations within the cortisol stress system—the hypothalamic-pituitary-adrenal (HPA) axis⁴—overactivity of which has been found in people with depression.^{w12}

The reasons for the high rates of relapse during pregnancy in those with a history of affective disorder have not been examined. Though any major life event is associated with an increased risk of relapse in those with affective disorders,^{w13} discontinuation of maintenance medication is probably a more specific and important contributory factor. A recent prospective study of women with a history of recurrent depression found that 68% of those who discontinued antidepressant medication after conception relapsed, compared with 26% of those who continued taking their medication without interruption.³

This is one of a series of occasional articles about how to manage a pre-existing medical condition during pregnancy. If you would like to suggest a topic for this series please email Kirsten Patrick (kpatrick@bmj.com)



CHLOE JOHNSON/LAWRY

Although women are at a low risk of suicide during pregnancy,^{w14} it is the most common cause of maternal death in the year after the birth.⁵

How does depression affect the outcome of pregnancy?

Studies examining obstetric complications in women who are depressed during pregnancy are difficult to interpret because the possible consequences of untreated depression are difficult to separate from the possible consequences of taking psychotropic medication. Some findings suggest that depressed pregnant women have an increased risk of complicated deliveries^{w15} or miscarriage,^{w16} but the latter tends to be associated with exposure to antidepressants during pregnancy.^{w17} There is more convincing, but inconsistent,^{w18} evidence of an association between antenatal stress and preterm delivery or low birth weight, or both,^{6 7 w19-w21} as in the case report presented here where the baby was born after 35 weeks' gestation. Most of these studies used various measures of psychosocial stress, but the associations with poorer birth outcomes were more evident when measures of depression were used.^{7 w21} The effects of depression on birth outcome are more evident in poorer countries^{2 w3} and among relatively deprived social groups in the economically developed world.^{w6 w10 w19} One of the most replicated findings is the poorer birth outcomes for African-American women compared with non-Hispanic white women.^{w6 w7} A study from Pakistan has shown that the negative effects of maternal antenatal depression on infant growth continue for at least a year after birth.²

There is evidence that antenatal depression may have a specifically harmful influence on development of the central nervous system. A large Danish study (n=20299 pregnancies) reported that an unexpected death during the first trimester was associated with an adjusted odds ratio of 8.36 (95% confidence interval 2.41 to 29.0) for cranial neural crest malformations in the babies born to these women.^{w22} This suggestion of a specific effect of maternal stress on brain development is supported by the finding of higher levels of behavioural disturbance at four years in children born to women with high anxiety scores during pregnancy.^{w23}

A unifying hypothesis explaining the association of both depression and social adversity on outcome of pregnancy is that the cortisol stress hormone system is a common mediating pathway.^{4 w11} Multiple stressors, including psychosocial stress, hunger, and infection, stimulate the secretion of cortisol during, and outside of, pregnancy.^{4 w12} Increased activity within the gestational cortisol system, via increased placental secretion of corticotrophin releasing hormone, has been shown to lead to premature delivery.^{4 w24} There is less evidence implicating increased noradrenaline secretion, resulting from maternal anxiety, as a possible causal agent.^{w25} Another mediating pathway between depression during pregnancy and poorer birth outcomes is the unhealthy behaviours associated with depression, such as smoking, alcohol and substance misuse, and poor attendance for obstetric care, all of which have adverse effects on pregnancy outcome.^{w26} Health risk behaviours seem to have a stronger effect on intrauterine growth, while psychological stress has a stronger effect on preterm delivery.^{6 w19}

How is depression treated in pregnancy?

Episodes of depression can vary from a mild syndrome to severe clinical states, as in the case described above. In milder states psychotherapy may be the preferred treatment. A small controlled clinical trial showed that interpersonal psychotherapy was effective,⁸ but psychotherapy services may not be immediately accessible and time to response is longer than with medication. In moderate depression an individualised approach, balancing the possible risk of exposure to medication against the possible adverse outcomes associated with discontinuation of medication, should be adopted.

Antidepressants are usually indicated in women with a history of severe or recurrent depression. There are no randomised controlled trials of treatment with antidepressants compared with placebo, and research has focused on examining the potential adverse neonatal outcomes associated with antenatal exposure to antidepressants. Two studies of population data have linked indices of mental health, prescriptions for selective serotonin reuptake inhibitors during pregnancy, and neonatal outcome.^{9 10} One of these reported a relative risk of congenital malformations in babies born to women taking selective serotonin reuptake inhibitors, but not tricyclic antidepressants, during the first trimester of pregnancy (1.34, 95% confidence interval 1.00 to 1.79).⁹ This increased risk, however, was not supported by a meta-analysis of prospective comparative cohort studies.^{w27} The second study reported a poorer obstetric outcome associated with maternal antenatal depression and the outcome was worst for women who were prescribed selective serotonin reuptake inhibitors.¹⁰ Another retrospective study suggests that exposure to these drugs in the third trimester is associated with persistent pulmonary hypertension of the newborn, but the absolute risk remains small (6-12/1000).^{w28} Compared with other antidepressants, paroxetine use during pregnancy is associated with an increased risk of congenital

malformations, particularly cardiac abnormalities.^{w29}

A serotonin withdrawal syndrome that is self limiting and usually managed with supportive care can occur in neonates exposed to selective serotonin reuptake inhibitors during pregnancy.^{w29 w30} This syndrome is variably described but common symptoms include hypotonia, irritability, excessive crying, sleeping difficulties, and mild respiratory distress. It is more likely to occur with paroxetine than with other drugs in the same class.^{w29}

What advice should be given about family planning?

Family planning should be discussed with all women who have an affective disorder and could become pregnant, regardless of reproductive plans. Women should be referred to specialist psychiatric services, if possible, for advice before they plan a pregnancy.^{w31} Women who are not at high risk of relapse should try to reduce their medication gradually before they embark on a pregnancy.^{w32} Explain the evidence and evaluate the risk on an individual basis so that women can make an informed choice about whether or not to take medication.

As pregnancy progresses

Women with a history of recurring depression or bipolar disorder should be referred to perinatal psychiatric services or, when such services are not available, to general psychiatric services for management during pregnancy. Such women should not abruptly discontinue maintenance medication if they discover they are pregnant.³ Regular assessment of mood state during pregnancy should be routine for all women as antenatal depression is unlikely to remit and is one of the most robust predictors of postnatal depression; about half of so called postnatal depression actually starts during pregnancy.^{1 w2 w11}

The practice of gradually discontinuing antidepressants during the third trimester in an attempt to minimise withdrawal effects in the neonate is controversial.^{w33} This strategy carries a potentially high risk of relapse during the third trimester and early postpartum period and does not rule out the possibility that the baby is experiencing withdrawal symptoms in utero.^{w31-w33} In our practice we advise breast feeding in the immediate postnatal period followed by gradual introduction of formula milk feeding as a strategy to reduce withdrawal phenomena.

Summary

Depression during pregnancy is a common problem and, as the case report indicates, is unlikely to remit unless it is actively managed. Untreated depression in pregnancy is associated with poorer maternal health practices and less favourable obstetric outcomes. Clinicians should ask about depressive symptoms as a routine part of antenatal care. If necessary, women should receive psychotherapeutic or psychopharmacological treatments, in the context of individual symptoms and risks. Women with an established history of mood disorder should be managed by specialist psychiatric services.

SUMMARY POINTS

Rates of depression are higher during pregnancy than at any other point during a woman's life

About half of "postnatal" depression starts during pregnancy

Two thirds of women with a history of recurrent depression will relapse during pregnancy if they discontinue their medications after conception

Depression during pregnancy is associated with poorer obstetric outcomes, particularly preterm delivery

Women who are depressed during pregnancy are more likely to smoke and drink alcohol and less likely to attend for antenatal obstetric care than women who are not depressed

The treatment of depression during pregnancy must be considered individually for each woman, with the possibility of relapse and poorer obstetric outcomes balanced against the possible risks associated with taking antidepressant medication

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Endpiece

A finding

One sometimes finds what one is not looking for.
Alexander Fleming

Submitted by Alistair Tindall, specialist registrar, London