

**Review Article**

**DEPRESSION IN PREGNANCY-CONSEQUENCES AND TREATMENT MODALITIES**

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**ABSTRACT**

Depression is a mood disorder which can affect 1 in every 4 women at some point of life even during pregnancy. Depression is most often not properly diagnosed during pregnancy as it is assumed by people to be just another type of imbalance in hormones. But this assumption can be very dangerous to the mother and the fetus. The health care professionals are very cautious about the treatment for depression in pregnancy as both uses of antidepressant and untreated depression in pregnancy can lead to risks for the unborn baby. This review focuses on the complications associated with both treated and untreated depression during pregnancy. In addition, if the treatment is inevitable, then factors such as teratogenesis, withdrawal symptoms, neurobehavioral effects, risk of untreated and risk of discontinuing the medication need to be considered before selecting the suitable therapy.

**Keywords:** Pregnancy, Depression, Drug-therapy, Fetal toxicity

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**INTRODUCTION**

Pregnancy is supposed to be one of the happiest moments in a woman's life, but many women face confusion, fear, stress and even depression during this time. Just like any other clinical depression, the depression during pregnancy is also a mood disorder. The hormonal changes during pregnancy can affect the chemicals in the brain, which is directly linked to depression [1]. The diagnosis of depression in pregnancy is most often not properly done as it is very difficult to differentiate between depression and other hormonal imbalance. Both untreated depression and use of antidepressants during pregnancy may have ill effects on both the mother and the fetus [2]. The depression during pregnancy and the postnatal period carries significant adverse effect on the mother as well as the offspring. Studies have found out that pregnant women who took antidepressants were more likely to have babies with reduced size of the head and had twice the chance of having a preterm birth compared to pregnant women who were not taking antidepressants. However, in contrast, pregnant women with untreated depression were more likely to have babies who had both smaller size of body and reduced fetal head growth [3]. Hence, this study was designed to find the complications associated with both treated and untreated depression in pregnant women and the factors that need to be considered while deciding the pharmacotherapy for depression.

**Prevalence of depression in pregnancy and possible triggers**

Depression is twice as common in women compared to men, and it frequently occurs during the childbearing time. The women with pre-existing depression are at a higher risk of getting depression during pregnancy and post-partum period. About 14-23% of women experience depressive symptoms during pregnancy [4].

The possible triggers for depression during pregnancy include [5]:

- Personal or family history of depression
- Any relationship problems
- Treatment for infertility
- Loss of previous pregnancy
- Complications in pregnancy
- Stressful events in life
- History of abuse or trauma

**Risk of maternal depression on the infant**

The presence of depression and the use of antidepressant medication during pregnancy is found to be associated with negative effects on the infants [6, 7]. The baby born to a depressed woman is found to be more agitated and less active and decreased attentiveness compared to the infant born to a woman without depression [8-10]. Untreated depression in pregnant women can cause premature birth, low birth weight and many other developmental problems in the fetus [11]. The postnatal depression in women can lead to poor cognitive and language development in the infant. They are found to have declined I. Q and insecure attachments. Postnatal depression in a mother can lead to negative parenting and suicidal behavior. They have a poor parent, child interaction [12, 13]. Research has found that the prevention on maternal depression can prevent infant problems of maternal depression-like behavioral problems, insecure attachments, etc.

**Signs of depression in pregnancy**

The pregnant women with depression may experience some of the following signs and symptoms for about two weeks or more [14, 15]:

- Persistent sadness
- Either sleeping too little or too much
- Difficulty in concentrating
- Loss of interest in activities that was usually enjoyed
- Feeling of worthlessness or hopelessness
- Recurring suicidal thoughts and death wishes
- Guilty feeling
- Change in the eating habits

**Treatment option for pregnant depressed women**

The various treatment options available for depressed pregnant women are [16, 5];

- Support groups
- Psychotherapy
- Medications
- Light therapy

- Lifestyle modifications

Due to the less availability of information regarding the safety and long-term effects of the use of antidepressant medications in pregnant women, many women are interested in other natural ways to treat depression.

A woman having mild to moderate depression can control her depressive symptoms with the help of support groups, psychotherapy, and light therapy and lifestyle modifications [17, 18].

- **Exercise-** It helps in increasing the serotonin levels naturally and decreases the cortisol levels
- **Adequate rest-** Establishment of a daily schedule for sleep greatly improves the body's and mind's ability to handle stress and daily challenges
- **Diet and nutrition-** Some foods like caffeine, sugar, artificial additives, and processed carbohydrates can lead to problems in mental and physical health. So a proper and healthy diet helps in managing depression.
- **Acupuncture-** Studies have found that acupuncture can treat depression in pregnant women to some extent. It is a practice in which tiny needles are placed into the areas in the body that are thought to influence the mood.
- **Light therapy-** In this therapy, the pregnant women is exposed to artificial lights at specific times of the day to help them relieve the depressive symptoms.
- **Omega-3 fatty acids-** It has many health benefits and recent studies have shown that taking a daily supplement of omega-3 fatty acids can decrease the symptoms of depression.
- **Herbal remedies-** many herbal supplements and vitamin supplements are available which can affect the mood and it can change the serotonin levels.

#### Choice of antidepressant in pregnancy

Severe depression in pregnant women needs a combination of psychotherapy and medications. While treating major depression, the benefits and risk of the medications should be clearly examined [19]. The drug, which provides maximum effect and less risk to the fetus, should be selected. The other factors that should be considered while starting or stopping of antidepressant drugs are:

- Teratogenicity
- Toxicity to the neonate or the withdrawal syndrome
- Neurobehavioral effects
- The risk of untreated depression in pregnancy
- The risk of discontinuing the medicine

#### Teratogenicity

The studies have shown that there is no teratogenic effect of selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs). There is no evidence to support that use of SSRI and TCA during pregnancy increased the chance of intrauterine fetal death or increased risk of major malformations [19, 20]. The recent studies have shown that there is a possible risk of birth abnormalities with the use of paroxetine, and there are chances of development of pulmonary hypertension with fluoxetine. SSRI's is found to be associated with decreased gestational age and low birth weight [21, 22].

#### Toxicity to neonate

There are many reports suggesting that the use of SSRI's, SNRI's during the late pregnancy is associated with neonatal withdrawal syndrome and poor neonatal adoption. The use of TCA during the third trimester was found to cause neonatal withdrawal effects like agitation, irritability, and seizures. But untreated depression during pregnancy can also predispose these problems [23, 24].

#### Neurobehavioral effects

Studies have shown that the infant born to the mother who was under Fluoxetine throughout the pregnancy showed no detectable ill effects on cognition, language development or temperament whereas the infant born to untreated mother was found to have poor cognition and language development [3]. The use of a tricyclic antidepressant during pregnancy had no effect on the I. Q, language development, cognition of the children, whereas untreated depression was found to be associated with poor cognition and language development in neonate children [24].

#### The risk of untreated depression during pregnancy

The studies have found a relationship between untreated depression in pregnancy and the adverse effects seen in the mother and the fetus. Maternal depression, acting as a stressor can affect the fetal development by its action on the hypothalamus, pituitary, adrenal and adrenocorticotropic hormones and the beta endorphins [25]. Postnatal depression of the mother is associated with problems like insecure attachment and declining I. Q in the child. The other adverse effect of untreated depression in pregnancy includes suicidal thoughts, inadequate self-care, abuse of substance, poor adherence to the prenatal care, spontaneous abortion, hypertension, pre-eclampsia, intrauterine growth retardation, preterm birth, low birth weight of the newborn, depressive behavior in the infant and postpartum depression [26].

#### Risk of discontinuing the medication

The discontinuation of the antidepressant medication can lead to increase in the risk of relapse of depression. The women who continued the medication throughout the pregnancy showed a lesser relapse rate compared to the pregnant women who discontinued the medication [27].

#### Antidepressants used

Depression is one of the most commonly seen mood disorder in pregnant women. The pregnant women with severe depression are given antidepressant drugs as untreated depression in pregnancy may lead to an adverse effect on the mother and the fetus. The relapse rate on discontinuing the medications is also high [27]. The use of antidepressants during the first trimester of the pregnancy is found to be associated with increased chances of miscarriage. The commonly used antidepressant drugs during pregnancy are selective serotonin reuptake inhibitors, serotonin/norepinephrine reuptake inhibitors, and tricyclic antidepressants.

Antidepressant therapy during lactation may also pose a problem as all the psychotropic drugs are found in the breast milk and is exposing it to the nursing infant. The commonly used antidepressant medications in postnatal women are SSRI's and SNRI's. Even though all the SSRI are found in breast milk, no serious adverse effect of its use has been found in children. The medications like citalopram and fluoxetine are found the highest compared to sertraline and fluvoxamine in breast milk [28]. There are no evidence suggesting the short-term toxic effect of TCA on infant other than doxepin and there are no long-term developmental adverse effects also. The preferred tricyclic antidepressant during breastfeeding is amitriptyline and imipramine.

#### Selective serotonin reuptake inhibitors and serotonin/norepinephrine reuptake inhibitors

This group of antidepressants are the most studied class of antidepressant for their use in pregnancy. Until 2005, SSRI was thought to be relatively safe for the use in pregnant women as there was no congenital anomalies observed compared to those not exposed to the antidepressants [28]. But in the recent year, there are many concerns regarding the safety of the SSRI as the drug paroxetine was suspected to increase the risk of structural malformations in fetuses', especially cardiac anomalies. The recent studies have shown that there is a significant relationship between the exposure to paroxetine prenatally and the risk of developing hypospadias [29]. The other SSRI like fluoxetine, sertraline and citalopram have shown to increase the risk of fetal cardiac defects, but the data available regarding escitalopram are reassuring. The

results of the studies done on the safety of use of venlafaxine during pregnancy showed no significant increase in the risk of teratogenic effect [30, 31].

The use of SSRI and SNRI during the late pregnancy has been associated with persistent pulmonary hypertension of the newborn. The other complications linked to the use of SSRI and SNRI in the late pregnancy are cardiac, respiratory, neurological, gastrointestinal and metabolic anomalies either due to toxicity or withdrawal phenomena. It is also associated with preterm birth and low birth weight. But in general, SSRI are the first-line drugs for the treatment of depression in pregnant women as more data are available about their safety compared to any other class of antidepressant medications [32].

### Tricyclic antidepressants

The tricyclic antidepressants act by increasing the availability of norepinephrine by blocking the reuptake of serotonin and by increasing the sensitivity of the postsynaptic neurons to serotonin. There is evidence available for the association of use of clomipramine and fetal cardiac defects, but there are no other definitive data regarding the safety of other TCA drugs [33]. There is an increased risk of developing prenatal antidepressant exposure syndrome in neonates exposed to the tricyclic antidepressants during the late stage of pregnancy.

### Other antidepressants

The other antidepressant drugs available are monoamine oxidase inhibitors, but they are less commonly used. MAOI's act by inhibiting the degradation of monoamine oxidase. This class of antidepressants is used for patients with refractory depression due to their poor safety and side effect profile.

### CONCLUSION

Depression is one of the most common mood disorder seen in pregnant women. Both the untreated depression and the use of antidepressant drugs may lead to an adverse effect on the mother and the fetus. The advantage of antidepressant therapy over the effects of untreated depression should be considered while selecting the treatment for depression in pregnancy. The treatment of depression in pregnant women is a challenge for the physician due to the ill effects that can occur to the fetus. While treating the depression in pregnant women the physician should consider the severity of the illness, the effect of medication on the fetus, the effect of withdrawal syndrome, the chances of relapse, etc. The lack of proper information regarding the safety of the anti-depressants drugs makes the treatment all the more difficult. Untreated depression can lead to developmental defects like poor cognition, poor language development and a sense of insecurity in the infant. The use of antidepressant drugs may cause some of the problems like pulmonary hypertension of the newborn, cardiac anomalies, low birth weight, etc. The infant whose mother was under antidepressant drugs showed better cognition, language development, I. Q, lesser agitation, lesser irritability compared to the infant of an untreated depressive mother. The SSRI and TCA drugs are relatively safe to be used during pregnancy, although it is recommended to reduce their dose the last trimester due to the risk of premature birth and low birth weight. With effective surveillance and management, the ill effects to the fetus due to the antidepressant use in pregnancy can be controlled. The toxic effects and withdrawal syndrome in the infants can be managed with proper follow-up and surveillance. The health care professional should be careful while treating the depression during pregnancy and lactation.

### CONFLICT OF INTERESTS

Declare none

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