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# ANTIDEPRESSANT THERAPY IN PREGNANCY AND THE POSTPARTUM PERIOD: MODERN STRATEGIES

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**Abstract**
Depression during pregnancy and the postpartum period is among the most common affective disorders in women of reproductive age, affecting up to 15%. It has a significant negative impact on both the mother's mental health and the child's development and well-being. Alongside psychotherapy, pharmacological methods—particularly antidepressants—play an important role in treatment. Despite concerns regarding the safety of antidepressants during pregnancy and breastfeeding, a growing body of research supports their effectiveness and relative safety when used appropriately.

## Introduction

Depression during pregnancy and the postpartum period is among the most common affective disorders in women of reproductive age, affecting up to 15%. It has a significant negative impact on both the mother's mental health and the child's development and well-being. Alongside psychotherapy, pharmacological methods—particularly antidepressants—play an important role in treatment. Despite concerns regarding the safety of antidepressants during pregnancy and breastfeeding, a growing body of research supports their effectiveness and relative safety when used appropriately.

Untreated depression is associated with a high risk of adverse outcomes, including impaired maternal functioning, suicidal thoughts and behaviors, difficulties in establishing an emotional bond with the infant, increased risk of delays in the child's cognitive and emotional development [16], as well as preterm birth and low birth weight [3]. It is important to note that the potential risks associated with antidepressant use are often significantly lower than the consequences of no treatment [16].

The primary goal of treatment during pregnancy is to minimize exposures—both medication-related and stemming from the disorder itself. In cases of planned pregnancy, it may be appropriate to switch from a less-studied medication to one with a more favorable safety profile, provided that the previously used drug was not ineffective.

In the case of an unplanned pregnancy, antidepressants should not be discontinued abruptly, as this may trigger stress, withdrawal symptoms, and relapse. Even if discontinuation is necessary, it should be carried out gradually, taking into account that exposure has already occurred. Decisions regarding treatment modifications must be balanced and clinically justified.



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The benefits of breastfeeding for the infant are well documented, and the American Academy of Pediatrics recommends maintaining breastfeeding for at least six months [22]. All antidepressants pass into breast milk to some degree. If the infant has already been exposed to an antidepressant in utero, it is generally not advisable to switch medications solely because breastfeeding has begun, except in the following situations:

1. The patient has experienced a relapse and the current treatment regimen is ineffective;
2. The woman is taking a medication associated with a high risk of serious adverse effects for the infant;
3. The infant shows signs of side effects or complications related to maternal medication use.

If there is a need to change the treatment regimen during breastfeeding, it is important to consider whether the additional risk of repeated drug exposure for the infant is justified. The decision should be made jointly with a pediatrician, who also participates in monitoring the infant's condition.

If the medication can be monitored through serum levels, laboratory testing in the infant may be acceptable. Common adverse effects may include sedation, drowsiness, and decreased appetite—particularly after the mother's dose.

It can sometimes be difficult to distinguish medication side effects from typical infant fussiness. In such cases, decision-making should be guided by what will provide the parents with a sense of safety and confidence.

**FDA Classification and New Regulations**

Until 2015, the U.S. Food and Drug Administration (FDA) used an alphabetical category system (A, B, C, D, X) to assess the risks of medication use during pregnancy. However, this approach proved insufficiently informative, as it did not reflect the breadth of available evidence, mechanisms of drug action, or the clinical context of their use. In 2015, a new rule—the Pregnancy and Lactation Labeling Rule (PLLR)—came into effect, requiring manufacturers to provide more detailed and structured information regarding potential risks and benefits of medication use during pregnancy and breastfeeding. Since the transition to the new system is still ongoing, knowledge of both the former letter-based classification and the current PLLR requirements remains essential in clinical practice.

Prescribing antidepressants in the perinatal period, including postpartum depression and lactation, poses particular challenges. In these clinical situations, physicians must consider not only the efficacy and safety of therapy for the mother but also the potential impact on the infant, despite the limitations of the evidence base and the need to account for the individual circumstances of each family.

To support clinicians in making well-informed decisions, specialized guidelines have been developed. For example, in 2017 the British Association of Psychopharmacology (BAP) published a consensus guideline on the use of antidepressants prior to conception, during pregnancy, and in the postpartum period [21]. This document, prepared with the involvement of experts in perinatal psychiatry, pharmacology, teratology, and child development, offers practical recommendations to help clinicians balance the risks and benefits of antidepressant treatment.

In preparing these recommendations, the updated national clinical guidelines of the National Institute for Health and Care Excellence (NICE CG192, 2014) were also taken into account,



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emphasizing the importance of shared decision-making. Clinicians are advised to discuss in detail with the patient and her partner the potential benefits and possible risks of pharmacological treatment, as well as to consider alternative management options.

Thus, modern approaches—including the updated FDA regulations and the PLLR system, as well as national and European clinical guidelines—highlight that, when chosen carefully and monitored appropriately, certain antidepressants may be used in women during pregnancy and in postpartum depression, including the lactation period, while minimizing risk to the infant and supporting the mother's mental health.

In this context, the aim of the present article is to analyze current evidence on the use of antidepressants during pregnancy, in the postpartum period, and during breastfeeding, with a focus on efficacy, potential adverse effects, safety considerations, and clinical monitoring that should be taken into account when prescribing therapy during this sensitive period.

## MATERIALS AND METHODS

A search was conducted in the PubMed, Scopus, Web of Science, and eLibrary databases using the following keywords: *pregnancy, antidepressants, SSRIs, tricyclic antidepressants, bupropion, congenital malformations, PNAS, safety, breastfeeding, women's mental health*. The search yielded 1,471 articles. Publications in English were included in the analysis, encompassing original research studies, systematic reviews and meta-analyses, cohort, longitudinal and cross-sectional studies, clinical practice guidelines, and regulatory documents that examined the safety and efficacy of pharmacotherapy for depression during pregnancy and the postpartum period, including breastfeeding.

After applying the appropriate inclusion and exclusion criteria, a total of 22 articles were selected for the final review.

## RESULTS

### ANTIDEPRESSANTS: EFFICACY AND SAFETY

Among psychotropic agents prescribed during pregnancy, antidepressants occupy a leading position in terms of frequency of use. To date, there is a substantial body of research evaluating their effects on the fetus and newborn. Although earlier publications reported potential adverse outcomes, many of those studies failed to account for the impact of the depressive disorder itself, which distorted the findings.

According to available data, for certain antidepressants—such as bupropion—observational studies have not demonstrated an association with serious congenital malformations [3,9,10]. Findings regarding tricyclic antidepressants are similar: most studies have not identified an increased risk of developmental defects [11]. Only one large epidemiological study reported a statistically significant increase in the risk of major malformations, estimating an odds ratio of approximately 1.36 (1.07–1.72). For other classes of antidepressants, existing data are limited but generally do not raise major safety concerns [6].

With respect to selective serotonin reuptake inhibitors (SSRIs), some publications have noted a slight increase in the probability of rare anomalies [4]; however, pooled findings from four meta-



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analyses focusing on first-trimester SSRI exposure do not support a statistically significant rise in the risk of major congenital defects [1,12].

When discussing the potential association between antidepressants and congenital heart defects, it is essential to account for confounding factors appropriately. Early studies suggested that SSRI use may be linked to increased rates of cardiac anomalies in infants [8]. However, it later became clear that these analyses compared women with depression to women without depression, making it impossible to isolate the effect of the medication itself. More recent data, based on large samples and more rigorous analytical methods, show that among women with major depressive disorder, SSRI use in early pregnancy does not increase the risk of congenital heart defects compared with those who did not take antidepressants. This suggests that previously reported associations between in utero antidepressant exposure and cardiac malformations may be attributable not to the treatment itself but to accompanying behavioral and social factors more common in women with depression.

A similar situation has emerged regarding the potential association between antidepressants and persistent pulmonary hypertension of the newborn (PPHN)—a severe condition in which the infant's pulmonary vessels fail to reduce vascular resistance after birth, leading to respiratory failure and requiring intensive treatment. The possible link between SSRI use and PPHN was first described in 2006 [7], prompting an official FDA warning and revisions to prescribing information for these medications. Subsequently, six additional studies were conducted: three found no evidence supporting this association [5], while two reported a relationship [17,18], although the estimated risks were lower than in the initial investigation. The largest study to date, involving nearly four million pregnancies, found no statistically significant increase in PPHN risk after adjusting for confounding factors [15].

Some studies suggest that in utero exposure to antidepressants may be associated with low birth weight, preterm birth, or even the development of autism. However, closer analysis shows that untreated psychiatric disorders themselves also affect these outcomes [16]. For example, women with untreated depression have higher rates of preterm birth and low-birth-weight infants, underscoring the impact of the disorder itself. A similar pattern is observed for the potential association between SSRIs and autism: if one accounts only for medication exposure without considering the mother's psychiatric condition, misleading conclusions may arise.

One risk, however, appears more consistently described in the literature: a moderate increase in the likelihood of spontaneous miscarriage with antidepressant use during early pregnancy. According to several studies, this risk is estimated with an odds ratio of approximately 1.4–1.6.

Particular attention should be given to the so-called Poor Neonatal Adaptation Syndrome (PNAS)—a transient cluster of symptoms that may be observed in infants whose mothers took antidepressants in late pregnancy. The first references to such a "withdrawal-like syndrome" appeared as early as the 1970s. It remains unclear whether PNAS is caused by withdrawal, a direct toxic pharmacological effect, or a combination of both. Descriptions and diagnostic criteria for this condition are not standardized, and research on its treatment, prevention, and long-term consequences is still insufficient.

Revisions to the FDA labeling for SSRIs and SNRIs acknowledge the possibility of PNAS when these medications are used in the third trimester. Reported manifestations include respiratory difficulties, cyanosis, episodes of apnea, seizures, temperature instability, feeding difficulties,



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vomiting, hypoglycemia, altered muscle tone, hyperreflexia, tremor, irritability, and persistent crying. As a precaution, gradual dose reduction before delivery is sometimes considered; however, this recommendation lacks sufficient scientific support and is not suitable for women with significant psychiatric symptoms.

Available data indicate that approximately one-third of newborns exposed to antidepressants in utero may exhibit symptoms consistent with PNAS, and the likelihood increases with polypharmacy, particularly when benzodiazepines are used concurrently. Nevertheless, there remains a need for more large-scale, high-quality studies to better characterize the syndrome and identify effective risk-reduction strategies.

At present, there is no adequate evidence to support routine tapering of antidepressants during the third trimester, especially in patients with moderate to severe psychiatric disorders. On the contrary, some women may require a dose increase in late pregnancy, as pharmacokinetic changes—such as increased volume of distribution—may reduce medication concentrations and lead to symptom relapse.

Overall, current evidence suggests that the use of antidepressants during lactation can be regarded as relatively safe: most studies demonstrate that drug concentrations in the infant's bloodstream are extremely low or undetectable [13]. Nevertheless, it is important to monitor for signs of excessive sedation, feeding difficulties, or sleep disturbances, although such adverse effects remain uncommon.

## CONCLUSION

Pharmacotherapy of depression during pregnancy and the postpartum period—particularly the use of antidepressants—is an effective and, when individualized, relatively safe treatment approach. Discontinuing therapy in favor of allowing the condition to progress "naturally" may result in far more severe consequences than the potential side effects of medication. Optimal outcomes are achieved through a multidisciplinary approach, informed consent, and careful monitoring of both mother and infant throughout the entire course of treatment.

## KEY POINTS

1. Antidepressants remain one of the most extensively studied and frequently prescribed classes of psychotropic medications for postpartum depression, including during pregnancy and breastfeeding.
2. Contemporary evidence indicates that, when benefits and potential risks are properly evaluated, the use of antidepressants is not associated with a significant increase in major congenital malformations, serious anomalies, or other severe outcomes.
3. Certain risks—such as spontaneous miscarriage or poor neonatal adaptation syndrome—require special attention and an individualized approach during treatment planning and management.
4. The best outcomes are achieved through a multidisciplinary approach, informed decision-making by the patient, and clinical monitoring of both mother and infant at all stages of treatment.



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**REFERENCES**

1. Alwan S., Reefhuis J., Botto L.D., Rasmussen S.A., Correa A., Friedman J.M. Maternal use of bupropion and risk for congenital heart defects // American Journal of Obstetrics and Gynecology. — 2010. — T. 203, № 1. — C. 52.e1–52.e6. — DOI: 10.1016/j.ajog.2010.02.015.
2. Alwan S., Reefhuis J., Rasmussen S.A., Friedman J.M. Patterns of antidepressant medication use among pregnant women in a United States population // The Journal of Clinical Pharmacology. — 2010. — T. 51, № 2. — C. 264–270. — DOI: 10.1177/0091270010373928.
3. Andrade S.E., McPhillips H., Loren D., Raebel M.A., Lane K., Livingston J., Boudreau D.M., Smith D.H., Davis R.L., Willy M.E., Platt R. Antidepressant medication use and risk of persistent pulmonary hypertension of the newborn // Pharmacoepidemiology and Drug Safety. — 2009. — T. 18, № 3. — C. 246–252. — DOI: 10.1002/pds.1710.
4. Byatt N., Deligiannidis K.M., Freeman M.P. Antidepressant use in pregnancy: a critical review focused on risks and controversies // Acta Psychiatrica Scandinavica. — 2012. — T. 127, № 2. — C. 94–114. — DOI: 10.1111/acps.12042.
5. Chisolm M.S., Payne J.L. Management of psychotropic drugs during pregnancy // BMJ. — 2016. — P. h5918.
6. Hanley G.E., Oberlander T.F. The effect of perinatal exposures on the infant: antidepressants and depression // Best Practice & Research Clinical Obstetrics & Gynaecology. — 2014. — T. 28, № 1. — C. 37–48. — DOI: 10.1016/j.bpobgyn.2013.09.001.
7. Huybrechts K.F., Bateman B.T., Palmsten K., Desai R.J., Patorno E., Gopalakrishnan C., Levin R., Mogun H., Hernandez-Diaz S. Antidepressant use late in pregnancy and risk of persistent pulmonary hypertension of the newborn // JAMA. — 2015. — T. 313, № 21. — C. 2142–2151. — DOI: 10.1001/jama.2015.5605.
8. Jarde A., Morais M., Kingston D., Giallo R., MacQueen G.M., Giglia L., Beyene J., Wang Y., McDonald S.D. Neonatal outcomes in women with untreated antenatal depression compared with women without depression // JAMA Psychiatry. — 2016. — T. 73, № 8. — C. 826–835. — DOI: 10.1001/jamapsychiatry.2016.0934.
9. Kieler H., Artama M., Engeland A., Ericsson O., Furu K., Gissler M., Nielsen R.B., Norgaard M., Stephansson O., Valdimarsdottir U., Zoega H., Haglund B. Selective serotonin reuptake inhibitors during pregnancy and risk of persistent pulmonary hypertension in the newborn: population based cohort study from the five Nordic countries // BMJ. — 2012. — T. 344. — P. d8012. — DOI: 10.1136/bmj.d8012.
10. McAllister-Williams R.H., Baldwin D.S., Cantwell R., Easter A., Gilvarry E., Glover V., Green L., Gregoire A., Howard L.M., Jones I., Khalifeh H., Lingford-Hughes A., McDonald E., Micali N., Pariante C.M., Peters L., Roberts A., Smith N.C., Taylor D., Young A.H. British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017 // Journal of Psychopharmacology. — 2017. — T. 31, № 5. — C. 519–552. — DOI: 10.1177/0269881117699361.
11. Meek J.Y., Noble L. Policy Statement: Breastfeeding and the Use of Human Milk // Pediatrics. — 2022. — T. 150, № 1. — DOI: 10.1542/peds.2022-057988.



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webofjournals.com/index.php/5

12. National Institute for Health and Care Excellence. Antenatal and postnatal mental health: Clinical management and service guidance. NICE Clinical Guideline CG192. — London: National Institute for Health and Care Excellence, 2014.
13. Payne J.L. Psychopharmacology in pregnancy and breastfeeding // Medical Clinics of North America. — 2019. — Т. 103, № 4. — С. 629–650. — DOI: 10.1016/j.mcna.2019.02.009.
14. Pearlstein T. Use of psychotropic medication during pregnancy and the postpartum period // Women's Health. — 2013. — Т. 9, № 6. — С. 605–615. — DOI: 10.2217/whe.13.54.
15. Reis M., Källén B. Delivery outcome after maternal use of antidepressant drugs in pregnancy: an update using Swedish data // Psychological Medicine. — 2010. — Т. 40, № 10. — С. 1723–1733. — DOI: 10.1017/s0033291709992194.
16. Romaine E., McAllister-Williams R.H. Guidelines on prescribing psychotropic medication during the perinatal period // British Journal of Hospital Medicine. — 2019. — Т. 80, № 1. — С. 27–32. — DOI: 10.12968/hmed.2019.80.1.27.
17. Ross L.E., Grigoriadis S., Mamisashvili L., VonderPorten E.H., Roerecke M., Rehm J., Dennis C., Koren G., Steiner M., Mousmanis P., Cheung A. Selected pregnancy and delivery outcomes after exposure to antidepressant medication // JAMA Psychiatry. — 2013. — Т. 70, № 4. — С. 436. — DOI: 10.1001/jamapsychiatry.2013.684.
18. U.S. Food and Drug Administration. Content and format of labeling for human prescription drug and biological products; requirements for pregnancy and lactation labeling. Final rule // Federal Register. — 2014. — Т. 79, № 233. — С. 72063–72103. — PubMed PMID: 25509060.
19. Wang S., [и др.]. Selective Serotonin Reuptake Inhibitors (SSRIs) and the Risk of congenital heart defects: A meta-analysis of prospective cohort studies // Journal of the American Heart Association. — 2015. — Т. 5, № 4.
20. Wilson K., Zelig C., Harvey J., Cunningham B., Dolinsky B., Napolitano P. Persistent pulmonary hypertension of the newborn is associated with mode of delivery and not with maternal use of selective serotonin reuptake inhibitors // American Journal of Perinatology. — 2010. — Т. 28, № 1. — С. 19–24. — DOI: 10.1055/s-0030-1262507.
21. Yonkers K.A., Blackwell K.A., Glover J., Forray A. Antidepressant use in pregnant and postpartum women // Annual Review of Clinical Psychology. — 2013. — Т. 10, № 1. — С. 369–392. — DOI: 10.1146/annurev-clinpsy-032813-153626.
22. Yonkers K.A., Wisner K.L., Stewart D.E., Oberlander T.F., Dell D.L., Stotland N., Ramin S., Chaudron L., Lockwood C. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists // General Hospital Psychiatry. — 2009. — Т. 31, № 5. — С. 403–413. — DOI: 10.1016/j.genhosppsych.2009.04.003.



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