

ORIGINAL PAPER

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Evidence in the diagnosis and treatment of postpartum depression: a narrative review

Evidencias en el diagnóstico y tratamiento de la depresión posparto: revisión narrativa

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ABSTRACT

Introduction: Postpartum depression is one of the most common medical complications associated with adverse short- and long-term perinatal outcome in the mother, infant, and family. **Objective:** To describe various diagnostic methods and therapies used for the management of postpartum depression and to analyze the recommendations generated by different scientific groups (maternal-fetal medicine, American College of Obstetrics and Gynecology, NICE guidelines, psychiatry, pediatrics). **Methodology:** Different search strategies were used in the databases Medline (via Pubmed), Scopus, Web of Science, Embase, Cochrane, OVID Psycho, from January 01, 2020 to February 01, 2023, using the keywords "postpartum depression", "antidepressants", "cognitive behavioral therapy", "interpersonal therapy", "mindfulness", controlled vocabulary. Two investigators independently reviewed study titles and abstracts. **Results:** About 14% of pregnant women develop postpartum depression. The most relevant risk factors are a history of anxiety, depression, history of psychiatric treatment, history of physical abuse, postpartum medical complications. **Conclusions:** One in seven patients (14%) develop perinatal depression. Tools such as the Edinburgh Scale should be applied to all pregnant women at their first prenatal check-up appointment, during the third trimester and in the postpartum period. There are several safe therapies that have demonstrated symptom reduction and decreased levels of relapse, with few side effects.

Key words: Pregnancy, Depression, postpartum, Drug therapy

RESUMEN

Introducción. La depresión posparto es una de las complicaciones médicas más comunes, la cual se asocia con resultado perinatal adverso a corto y largo plazo en la madre, el infante y la familia. **Objetivo.** Describir diversos métodos diagnósticos y diversas terapias utilizadas para el manejo de la depresión posparto y analizar las recomendaciones generadas por las distintas agrupaciones científicas (medicina materno-fetal, Colegio Americano de Ginecología y Obstetricia, NICE guidelines, psiquiatría, Pediatría). **Metodología.** Se crearon diversas estrategias de búsqueda para las bases de datos Medline (vía Pubmed), Scopus, Web of Science, Embase, Cochrane, OVID Psycho, desde el 01 de enero del 2020 al 01 de febrero del 2023, utilizando las palabras clave "postpartum depression", "antidepresivos", "terapia cognitivo conductual", "terapia interpersonal", "mindfulness", vocabulario controlado. Dos investigadores examinaron de forma independiente los títulos y resúmenes de los estudios. **Resultados.** Alrededor de 14% de las embarazadas desarrollan depresión posparto. Los factores de riesgo más relevantes son antecedentes de ansiedad, depresión, antecedentes de tratamiento psiquiátrico, historia de abuso físico, complicaciones médicas posparto. **Conclusiones.** Una de cada siete pacientes (14%) desarrollaron depresión perinatal. Se debe aplicar herramientas como la Escala de Edimburgo a todas las gestantes en su primera cita de control prenatal, durante el tercer trimestre y en el posparto. Existen diversas terapias seguras que han demostrado reducción de los síntomas y disminución en los niveles de recaída, con pocos efectos secundarios.

Palabras clave. Embarazo, Depresión posparto, Farmacoterapia

INTRODUCTION

Postpartum depression (PPD) is a major psychiatric disorder that can occur during the first year after childbirth. It has a prevalence between 15%-20% in women in developing countries⁽¹⁾ and has become a social and health problem in recent years. In Panama, a prevalence of 10% has been estimated when patients in the first days of puerperium were studied, which translates into 1 out of every 10 women who give birth⁽¹⁾.



During this period, it is necessary to differentiate the very common baby blues which occurs in approximately 8 out of 10 women. It is characterized by symptoms of loneliness or mild sadness that do not exceed ten days. On the other hand, in PPD the condition lasts more than fourteen days and negatively affects the quality of life of the mother and baby⁽²⁾. It is associated with the absence or lack of mother-child attachment, decreased maternal responsiveness and higher rates of behavioral and clinical problems in the children of mothers with PPD⁽³⁾, as well as alterations in the emotional and cognitive development of the infant^(4,5).

The birth of a baby is known to be an important trigger for depressive episodes in some women. A history of mood disorders makes patients more vulnerable⁽⁶⁾. The rapidity with which the new changes occur and the lack of adaptability to them and to this new lifestyle of caring for the baby causes fatigue, lack of sleep, among other factors⁽⁷⁾. In turn, low self-esteem, anhedonia, appetite alterations, insomnia and constant moodiness can be found in the mother.

Important factors in the development of postpartum depression are anxiety, history of psychiatric illness, social isolation, low self-esteem, socioeconomic status, history of physical abuse, postpartum medical complications, family history of PPD^(8,9)(see Table 1).

After a few months, most women with postpartum depression recover. However, 30% of patients may take up to more than a year to show improvement.

DSM 5 does not specifically include postpartum depression as a separate diagnosis. However, it does refer to the term peripartum-onset major depression, defined as depressive symptoms occurring during pregnancy and 4 weeks after birth.

The diagnosis of PPD is complicated and overlooked because clinical manifestations such as fatigue, weight loss, decreased libido, insomnia, are also attributed to normal changes in pregnancy and the postpartum period⁽¹⁰⁾.

The aim of the present study is to describe the various diagnostic methods and therapies used for the management of postpartum depression according to the literature reviewed.

TABLE 1. RISK FACTORS ASSOCIATED WITH POSTPARTUM DEPRESSION.

Psychological	Previous history of depression
	Anxiety
	Low self-esteem
	Parental stress
Obstetrical	Multiparity
	High risk pregnancy
	Intrapartum complications (meconium passage, umbilical cord prolapse, hemorrhages)
	Low weight fetus
	Cesarean section
Biological	Gestational diabetes
	Young age
	Nutritional deficiency
	Maternal age
Social	Lack of emotional support
	Domestic violence
	Low socioeconomic level
	Low educational level
Lifestyle	Smoking
	Sleep deprivation
	Low physical activity
	Bad nutrition

METHODOLOGY

A narrative review was conducted on the diagnosis and treatment of postpartum depression. Several search strategies were created with keywords, MESH, free texts, using Boolean operators (AND and OR). A polyglot translator tool was used to evaluate the translation of each of the search strategies in the various databases. The search time was between January 1, 2020, and February 1, 2023, and there was no language restriction. An example of the search generated in PubMed is shown in the supplementary material.

RESULTS

MANAGEMENT

For the management of patients with postpartum depression, postpartum symptoms should be identified, which are depressed mood, anhedonia, sleep disturbances, psychomotor retardation, excessive feelings of guilt or decreased concentration, which should last about 2 weeks or more after delivery.



The first step in the management of a woman with postpartum depression is to assess the severity of her depression and determine whether it poses a threat to herself or others⁽¹¹⁾.

Patients with severe symptoms, such as suicidal ideation with a specific plan and intent for suicidal behavior, or auditory hallucinations, should be referred to an emergency department and obtain a psychiatric consultation for further evaluation and necessary immediate management, as well as protective measures for both mother and newborn. In severe cases of postpartum depression, especially in mothers who are at risk of suicide, hospitalization should be considered⁽¹¹⁾.

SCREENING METHODS

Early screening during pregnancy allows not only to identify women at risk who do not show symptoms, but also those who already show subclinical symptoms of depression⁽¹²⁾. It has been observed that the lack of timely treatment in a mother with postpartum depression increases the risk of smoking, substance abuse, dissatisfaction and guilt in the mother⁽¹³⁾. Women with untreated depression during pregnancy are at increased risk for postpartum depression.

EDINBURGH POSTPARTUM DEPRESSION SCALE (EPDS)

The Edinburgh Postpartum Depression Scale (EPDS) is widely used as a screening method. This scale, recommended by the American College of Obstetrics and Gynecology (ACOG), has proven to be an accessible instrument for the initial screening and follow-up of postpartum depression. The EPDS is a self-assessment questionnaire consisting of ten brief questions related to symptoms such as: anhedonia, guilt, anxiety, panic attacks, exhaustion, sleep disturbances, sadness, crying and suicidal thoughts. Each question has a rating from zero to three, where the sum of points equal to or greater than 10 reflect symptoms of postpartum depression, while a score greater than or equal to 13 represents a high risk of developing postpartum depression. This scale can be used 6 weeks before delivery and 6-12 weeks postpartum⁽¹⁴⁾.

One of the advantages of this scale is the possibility of identifying suicidal thoughts, even when the overall EPDS score is low⁽¹³⁾.

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

The PHQ-9 is an instrument used for screening, diagnosing, monitoring, and rating the severity of depression. This scale has 9 questions, which are scored from "0" (not at all) to "3" (almost every day), providing a severity score from 0 to 27. High scores are related to a diminished functional status, with symptomatology and need for medical attention.

The last question on this questionnaire, "How difficult have these problems made it for you to do your job, take care of things at home, or get along with other people?" is not included in the score, but it is a good indicator of the patient's overall status and can be used for follow-up. Because anxiety occurs in more than 37% of patients with depression, it is important to assess anxiety symptoms.

BECK DEPRESSION INVENTORY (BDI)

The Beck Depression Inventory (BDI) consists of 21 statements that consider the patient's mood. It focuses on items such as depressed mood, loss of appetite, sleep disturbances, suicidal tendencies, among others⁽¹⁵⁾.

It is used to quantify depressive symptoms as well as their intensity. A study that evaluated the accuracy of screening tests for the detection of postpartum depression detailed that there were notable differences in the tools included. Tools such as the EPDS focus their questions on feelings of sadness or anxiety, while others such as the Beck Depression Inventory and PHQ-9 focus on physical symptoms, such as fatigue, loss of energy, and changes in sleep routine⁽¹⁶⁾.

Among the different tools for the detection of postpartum depression, one of the most recognized tools for the prevention of depression is the Australian Beyond Blue Program. This program is an initiative to increase public awareness of early responses to depressive behavior. It aims to prevent postpartum depression and to provide recommendations if it has already set in⁽¹³⁾.

The literature indicates that educating the patient about postpartum depression promotes early recognition of symptoms, which is beneficial when choosing a form of treatment. Many



treatments in randomized trials have been identified as effective in reducing the prevalence of this disorder, including psychotherapy and certain medications⁽¹⁷⁾.

Mindfulness-based cognitive therapy focused on the treatment of postpartum depression is one of the few preventive measures proven to be effective in reducing the risk of this disorder in women with a known history of depression. Such therapy is based on a set of preventive interventions that promote coping skills and habits that increase susceptibility to depression, stress tolerance and awareness⁽³⁾.

The first-line drugs for treating postpartum depression are the so-called selective serotonin reuptake inhibitors (SSRIs), which have a low risk of toxicity and are less associated with severe adverse effects. So far, the SSRI drugs that have been most studied in clinical trials are sertraline and fluoxetine⁽¹⁷⁾.

EFFECT OF COVID-19 ON POSTPARTUM DEPRESSION

A study found a 34% increase in the prevalence of postpartum depression worldwide during the COVID-19 pandemic, values much higher than those reported prior to this event, ranging from 12% in developed countries to 25% in low- and middle-income countries. The various studies reviewed show high prevalences in countries such as Mexico (39%), Colombia (30.4%), Iran (32%), Canada (37%), Turkey (56%) and Spain (58%), i.e., between 5%-15% increase in prevalence compared to the years prior to the COVID-19 pandemic⁽¹⁸⁾. Risk factors for postpartum depression during the pandemic were defined as sociodemographic and clinical characteristics, such as stress, anxiety, lack of support, among others. The research findings indicate that the pandemic may have detrimental effects on maternal mental well-being after childbirth. As an acute public health problem, the COVID-19 pandemic required ongoing, comprehensive, and long-term health education to effectively alleviate women's panic and fear, thereby improving the mental well-being of this vulnerable population⁽¹⁹⁾.

Despite the severe consequences that postpartum depression has on the mother-child pair, up to 50% of cases are misdiagnosed or even never diagnosed⁽¹⁶⁾.

PHARMACOLOGICAL TREATMENT

Although many randomized clinical trials have not been convincing, pharmacological interventions consist of the administration of antidepressants such as selective serotonin reuptake inhibitors (SSRIs). SSRIs are used because they have been found to have the lowest risk of toxicity with respect to possible overdose and have fewer associated adverse events⁽²⁰⁾.

Some of the disadvantages of antidepressants is the concern on the part of the mother to develop adverse events. Many mothers prefer to avoid medications during the breastfeeding period and choose psychotherapy. SSRI antidepressants, such as sertraline or paroxetine, are usually recommended since they have a short half-life⁽²¹⁾. Citalopram and escitalopram are also recommended, based on their effectiveness and safety during breastfeeding⁽¹³⁾.

One of the major concerns of mothers is the level of the drug that may be present in the milk at the time of breastfeeding. It has been observed that sertraline has 98% binding to plasma proteins, which reduces the probability of transfer to milk. For this reason, and because sertraline levels in the infant's blood are practically undetectable, it is one of the most commonly used drugs in mothers with postpartum depression during lactation⁽²²⁾. See Table 2.

An analysis of 67 studies evaluating sertraline levels in infants, taking into account 238 infants showed that an average sertraline level of 45 mcg/L (range 7-207 mcg/L) could be expected in the breast milk of mothers ingesting a daily dose of 83 mg (range 25-200 mg). It was observed that these infants receiving approximately 0.5% of the dose of sertraline ingested by the mother (adjusted to their weight) showed low risk of adverse events⁽²³⁾.

It should be noted that the use of antidepressants has been associated with an increased risk of developing withdrawal syndrome, with tremor, increased muscle tension, sleep disturbances, or loud crying. However, these symptoms usually resolve spontaneously and do not require any specific treatment⁽²²⁾.



ALLOPREGNANOLONE

Allopregnanolone is a progesterone metabolite and neuroactive steroid (NAS) that acts as a positive allosteric modulator of the GABA-A receptor (PAM). GABA is an inhibitory neurotransmitter in the brain that is present in 30%-50% of neurons⁽²⁴⁾.

Allopregnanolone levels increase during pregnancy, leading to dysregulation of aminobutyric acid A (GABA-A) receptors. After delivery, estrogen and allopregnanolone levels fall rapidly during the first 3 days, reaching pre-pregnancy levels. GABA-A receptors take time to adapt to these lower levels. Sensitivity to these changes has been implicated in the etiology of postpartum depression⁽²⁵⁾.

The most convincing evidence for the role of allopregnanolone in postpartum depression comes from the strong antidepressant effects demonstrated in clinical trials with an allopregnanolone analog in postpartum women^(26,27).

NON-PHARMACOLOGICAL TREATMENT

Non-pharmacological interventions consist of psychotherapy, physical activity and psychosocial therapies, used individually or in conjunction with pharmacotherapy. Psychotherapy is especially recommended for women with low drug credibility or concern about drug use during lactation or fear of becoming addicted to these drugs⁽²⁹⁾.

According to some authors, psychosocial strategies such as peer support and counseling are recommended for mild depression. For moderate depression psychotherapy is advised and for severe depression antidepressants such as SSRIs⁽¹²⁾.

Recommendations for the treatment of mild to moderate depression in pregnancy based on

the results of some meta-analyses indicate the effectiveness of cognitive-behavioral therapy (CBT) or interpersonal therapy (IPT), both individually and in groups⁽¹³⁾.

MINDFULNESS

Mindfulness or detached mindfulness (DM) is a breakthrough in mental health research. This mindfulness offers a potential effective approach to the treatment of emotional distress and has been used with a variety of problems including stress, symptoms of depression, anxiety and distress.

Mindfulness is considered to originate from the practice of Eastern introspective spirituality, primarily Buddhism. As described it means 'paying attention with patience and care to what is going on around you', and this can be achieved through meditation. It has been described as an 'awareness focused on the present, without prejudice, in which every thought, feeling or sensation that arises in the attentional field is recognized and accepted as it is'. Mindfulness has been shown to be effective as an intervention to reduce depressive symptoms in many populations⁽³⁰⁾.

A meta-analysis that included 9 studies of adults with depression (75% women) documented a significant reduction in the risk of relapse over a 5-year follow-up period for those who received a mindfulness-based intervention compared with those who did not. Another meta-analysis based on 8 randomized controlled trials of pregnant women concluded that women in the in-person mindfulness arm experienced significant reductions in depression⁽³¹⁾.

Despite its good results, mindfulness training requires 30 or more hours of in-person instruction, with 45 minutes of daily homework, which limits adherence because mothers must take care of their babies or attend work; a good option would be virtual mindfulness therapies.

A recent meta-analysis of versions of virtual sessions based on traditional mindfulness interventions (e.g., mindfulness-based stress reduction) demonstrated significant benefit in terms of reduced stress, anxiety, depression, and well-being⁽³²⁾.

TABLE 2. ADVERSE EVENTS RELATED TO SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs).

Mother	Fetus
Dependence	Abstinence syndrome
Overdose toxicity	Tremor
	Increased muscle tension
	Sleep disorders
	Loud crying



COGNITIVE-BEHAVIORAL THERAPY (CBT)

CBT is a type of psychotherapy in which you work with a mental health counselor, either a psychotherapist or therapist, in a structured way and attend a limited number of sessions. This therapy helps patients become aware of negative thoughts so that they can see challenging situations more clearly and respond to them more effectively. It is based on the principle that if people can learn to evaluate their thoughts and change them in a more realistic and adaptive way, they can improve their emotional state and behavior⁽³³⁾.

In most cases, CBT focuses on the mother's relationship with her child, helping her to get a better handle on her new role as a mother and making her develop different skills⁽²¹⁾.

This intervention is often carried out in a group or individual setting for 12 weeks, and focuses on understanding the bond between mother and baby. It is based on identifying pleasant activities and moods, pleasurable activities that benefit the mother and baby, healthy thoughts about the mother and baby, learning to obtain social support, and using the course to create a better life for the mother and baby⁽³⁴⁾.

It has been observed that when it comes to CBT for postpartum depression, group CBT is more beneficial compared to individual CBT. However, the individual CBT experience is more effective in the first three months compared to group CBT⁽³⁵⁾.

A meta-analysis that included 26 CBT-related treatment studies found a significant effect for CBT across a variety of implementations; 20 of these addressed postpartum depression and 6 addressed prenatal depression. CBT was offered individually as well as in group settings. In the 26 studies reviewed, 16 of them showed a significant effect using CBT relative to the control group. There was no significant benefit of individual CBT relative to group CBT⁽³⁵⁾.

INTERPERSONAL THERAPY (IPT)

IPT is a type of short-term psychotherapy that focuses on interpersonal relationships, developed specifically for depression⁽¹⁵⁾. It was developed as an intervention that could be used as

an adjunct to pharmacotherapy. Practically, it is based on the concept that patients with depression usually develop social problems, which could result in interpersonal conflicts, problems in role transitions, or problems in loss management.

In the context of postpartum depression, the mother may develop interpersonal problems with her partner, feeling lack of support, lack of solidarity and lack of understanding. In this situation, IPT would focus on identifying the source of the conflict and the goals they have as a family, developing communication strategies.

In a meta-analysis they included a study based on women with a diagnosis of major depression who were randomized to a 12-session course of IPT or 12 weeks of waiting (as a control group). A total of 120 women were recruited, of whom 99 were ultimately included. Based on Beck scale scores, a highly significant difference was found in post-treatment patients. It was also observed that women who received IPT were able to significantly decrease conflict in their marriages with respect to the control group⁽³⁵⁾.

Two specific interventions, interpersonal therapy based on the ROSE (Reach Out, Stay Program Strong, Essentials for Mothers of Newborns) program and the Mothers & Babies program based on cognitive behavioral therapy decreased rates of perinatal depression compared with the control groups.

Finally, in June 2023, the American College of Obstetricians and Gynecologists has published a comprehensive guideline on the care of patients with mental illness during pregnancy and the puerperium⁽³⁶⁾.

CONCLUSION

Two out of 10 patients may develop postpartum depression. Tools such as the Edinburgh Scale, the PHQ-9 or the Beck Inventory Scale should be administered to all pregnant patients at their first prenatal visit, during the third trimester and postpartum. There are several safe therapies that have demonstrated symptom reduction and decreased levels of relapse with few side effects, including cognitive behavioral therapy, mindfulness and pharmacological therapies, in cases of severe postpartum depression.



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