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Abstract

Postnatal depression is the most common psychopathological disorder during the postnatal period. It is a mood and anxiety disorder and affects around 15 % of mothers. It involves the development of a major depressive episode whose onset can occur during pregnancy or within 4 weeks of giving birth, and depressive symptoms must be present for at least 2 weeks, but in clinical practice it is considered that it can also have an onset from pregnancy to 3–6 months postpartum, although it is more common during the postpartum period.

There are still many cases of postnatal depression that are not detected in clinical practice; in spite of that, it has deleterious consequences for the mother and for the baby and can delay the physical, social, and cognitive development of the baby.

Social, psychological, and biological factors can contribute to the development of postnatal depression. It is important to educate both professionals and mothers about the risk factors for early detection to prevent depression from developing.

The treatment of depressed women in the postpartum period may be different according to the characteristics of every clinical case; psychotherapy or pharmacotherapy may be used alone or in combination. The therapy may be beneficial for the symptoms and drug treatment is a good option in cases where postpartum depression is considered moderate or severe and in which therapy was not effective.

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20.1 Introduction

Even though women have the same prevalence of psychiatric disorders as men in most countries, there are differences in the psychiatric diagnosis made by sex. Epidemiological studies show rates of depressive and anxiety disorders twice as high in women compared with men. Biology explains some differences in the diagnosis, but mental illnesses are influenced by both biological and psychosocial factors.

The rates of depressive disorders increase in women during maternity. Throughout the whole postpartum period the risk of suffering them is particularly high considering that the mother suffers stressful and important changes physically and also in her surroundings, for example, during the breastfeeding period and transformation in the couple relationship and in the familial structure [1]. Postnatal depression (PND) creates negative outcomes in the mother, her partner, and in the newborn; thus, early detection and treatment nowadays must be a priority for public health.

20.2 Depressive Disorders in the Perinatal Period

Gestational depression and PND are the most common psychopathological disorders during pregnancy and the postnatal period they are mood and anxiety disorders. There are different forms of depression, from minor and temporary episodes of sadness to more severe and persistent forms.

On the one hand is gestational depression that is suffered by 14–23 % of the pregnant women [2], of whom 3 to 5 % are such severe cases that if they do not receive any treatment they can get worse after delivery [3]. For women with a history of major depression the risk of relapse during pregnancy is high, especially if pharmacological treatment has ceased [4].

Postpartum dysphoria occurs in about 50 % of births [5]. It is a transitory mild condition that remits naturally and usually does not require treatment. It appears in the first hours after childbirth and can last a few weeks, but if it lasts more than 2 weeks, and if there is a history of recurrent depressive episodes, it requires an evaluation to rule out the development of a more severe mood disorder.

Postpartum depression, which we focus on in this chapter, affects around 15 % of mothers and can appear in the first few weeks and even for up to a year after childbirth. Medical, psychological, and pharmacological intervention is required so as not to affect the ability of the mother to care for her child.

Postpartum psychosis is a severe disease with an incidence of 0.1–0.2 % [6] that may appear in the first weeks after birth and has an abrupt start and evolves quickly. The characteristic symptoms are depressed or exalted mood, behavioral maladjustment, emotional lability, delusions, and hallucinations. Medical, psychological, and pharmacological interventions are important to avoid it evolving into a major psychiatric disorder.

20.3 Symptoms and Prevalence

In 2013 The American Psychiatric Association changed the name of this condition to peripartum depression in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5). This involves the development of a major depressive episode whose onset can occur during pregnancy or within 4 weeks of giving birth [7] and, as in other major depressive episodes, depressive symptoms must be present for at least 2 weeks. However, in clinical practice it is considered that postpartum depression can also occur from pregnancy to 3–6 months postpartum [8, 9], although it is more common in the postpartum period.

The clinical symptomatology is characterized by sadness, anhedonia, tearfulness, fatigue, and anxiety. Also, eating and sleep disorders, loss of energy, and feelings of guilt commonly associated with the care of bringing up a child may appear. These symptoms are also observed in the ordinary postpartum period, which makes diagnosis more difficult. Therefore, it is recommended to explore for more specific symptoms such as impaired concentration, thoughts of death or self- or hetero-aggressiveness toward the newborn. Postnatal depression must be carefully distinguished from both normal and other postpartum psychiatric disorders common in this period, among which postpartum dysphoria and puerperal psychosis deserve social attention.

Each year PND occurs in between 15 and 20 % of all women of childbearing age, resulting in approximately 600,000–800,000 cases annually, and is one of the most common postpartum complications [10]. However, the prevalence is highly variable; some studies found rates from 0 to almost 60 % [11] and the rates vary between countries and within them [12].

20.4 Screening

Postnatal depression can be effectively treated and prevented [13], but there are still many cases continuing undetected in clinical practice [14]. Several tools for detecting depression exist, but few studies have evaluated their use in the postpartum period. The most commonly used in the scientific literature has been the Edinburgh Postnatal Depression Scale (EPDS) [15], a 10-item self-report scale to detect depressive symptoms in women who have just given birth that takes into account the severity of symptoms present during the previous 7 days. It has been translated into several languages and has been used both in clinical practice and in epidemiological studies [16, 17]. It has demonstrated its validity and reliability in several studies and has been recommended as a screening tool indicating the possible presence of depression in women after birth [18], but not as a diagnostic tool. The diagnosis of PND is made by detailed exploration of signs and symptoms in the context of the clinical interview as the Post-Partum Depression (PPD) must be distinguished both from normal puerperium and from other common psychiatric disorders in this period such as postpartum psychosis and postpartum dysphoria.

20.5 Etiology and Risk Factors

Social, psychological, and biological factors can contribute to the development of PND. However, most of the existing literature is focused on the social and psychological causes rather than on the biological ones.

20.6 Biological Factors

During pregnancy and postpartum, women experience hormonal changes, which are aimed at preparing the organism for both childbirth and the breastfeeding period. These changes affect the hormones and the neurotransmitters. Despite the fact that they are necessary to ensure the health of the women during this period, occasionally these alterations provoke deterioration in women's mental health after childbirth.

The concentration in plasma of hormones such as estrogens, progesterone, testosterone, cortisol, and corticotrophin-releasing hormone increases during the 40 weeks of pregnancy, decreasing drastically during childbirth [19, 20]. Several research works indicate that those hormonal changes can cause depression in a subgroup of vulnerable women. However, the origin of this sensitivity has not yet been clarified [21].

Alkistis Skalkidu [22] describes the biological changes associated with the development of postpartum depression, including elements such as the gonadal steroids, the hypothalamic–pituitary–adrenal (HPA) axis, the serotonergic neurotransmitter system, the thyroid system, inflammatory markers, and genetic risk factors.

20.6.1 Gonadal Steroids

Since progesterone and estradiol decrease rapidly after childbirth, their possible implications in the development of the PND have been studied often. In addition, low levels of estrogens have been associated with a reduction in a woman's well-being, and with the onset of depression after childbirth.

In more than 60 % of the cases of women with PND antecedents the low production of endogenous hormones has been linked to the emergence of depressive symptoms [23]. Some research works also corroborate that high-level estradiol treatments improve PND [24, 25]. On the other hand, there are studies that question the hypothesis of hypoestrogenism, as some evidence shows that women suffering deep depression sometimes have higher estradiol serum concentrations than mothers affected by PND in the early postpartum period [26].

As far as progesterone is concerned, in most of the cases it has been associated with postpartum dysphoria [27, 28]. However, in PND the evidence is not strong enough. Some research states that the decrease in progesterone levels coincides with the highest peak of the depressive symptoms in the early postpartum period.

Other studies, on the contrary, show no change [29], or even an increase in the progesterone [30].

Finally, Lawrie et al. [31] carried out a randomized, double-blinded, placebo-controlled clinical trial that demonstrated that the administration of progestogen in the early postpartum increases the risk of PND.

20.6.2 Hypothalamic–Pituitary–Adrenal Axis

The hormonal secretion system works in interrelationship with both the nervous and the immune system. External agents also affect it. During depression there are alterations in the operation of the HPA axis [32]. These three glands, namely, the hypothalamus, the pituitary, and the adrenal glands, operate in a synchronized way thanks to a feedback system. In specific types of depression this self-regulation system does not work. As a consequence the level of hormone production is higher than normal.

The alterations in the HPA axis observed in deep depression and during pregnancy and childbirth are similar to those mentioned above. In this way, the concentration of cortisol increases both in plasma and in urine [21].

A different origin and evolution of depression during pregnancy and in the PND have been pointed out. Thus, normally in the PND, the HPA axis reduces its activity [33], while in the depression suffered during pregnancy there is hyperactivity. Some studies demonstrate how women with PND have a reduced response capacity of the HPA axis compared with the controls [34, 35].

20.6.3 Other Factors in the Etiopathogenesis of PND

The activation of the inflammatory response system can be involved in the pathophysiology of PND [36]. This hypothesis states that external stressors, such as psychosocial factors, and internal stressors, such as organic inflammatory conditions that occur during the postpartum period, can trigger depression through the inflammatory processes [37, 38].

Oxytocin has been linked with childbirth and the breastfeeding period [39], suggesting that it has a positive effect on the mood [40]. The role of oxytocin in the mother–child attachment and social–cognitive processes has been highlighted [41]. These studies are addressed at searching for biomarkers, which, associated with the behavior of mothers affected by depression, could condition the development of the child.

A subgroup of the PND is founded in thyroid dysfunction. Up to 7 % of new mothers experience alterations in the thyroid system during and after childbirth compared with 3–4 % of the general population [42]. In addition, there is evidence that links thyroid dysfunction during pregnancy to depression in the first year after childbirth [43]. Therefore, the evaluation of the thyroid performance in the early

period after childbirth is important in order to monitor effectively the women at risk.

The serotonergic system plays a fundamental role in mood disorders and in PND treatment. The use of selective serotonin reuptake inhibitors (SSRIs) has been shown not only to be effective in PND, but also to be well tolerated by the mothers. However, this treatment has not been demonstrated to be well above any other treatments [44].

Epigenetics, genetics, and stress–environment interaction, including the interactions in the early development of their own mother, are factors that have an influence on the propensity for developing PND [45]. Long-term monitoring of the children whose mothers suffered PND shows that they have a tendency to be depressed that is four times higher than the rest of the population [46]. This fact suggests an intergenerational transference that increases the propensity for depression and PND in the descendants. Apparently, multiple genes play an important role in this vulnerability, but not many studies have researched this subject [47, 48].

20.7 Psychosocial Factors

All women are prone to developing depression following childbirth; however, women who have certain risk factors are at a significantly increased risk of experiencing the illness. Many investigators have already described various risk factors with differing views on their importance. In this sense, Robertson et al. described different categories of risk factors.

20.7.1 Strong to Moderate Risk Factors

Depression or anxiety during pregnancy: Experiencing depressed mood or anxiety during pregnancy was a significant predictor of postpartum depression [49–52] and higher levels of anxiety during pregnancy predict the level of postpartum depressive symptomatology.

Past history of psychiatric illness: Having previously experienced depressive symptoms at any time, not just related to childbirth [49–51, 53] leads to a significantly increased risk of postpartum depression.

Life events: Strong–moderate relationship between experiencing a life event and developing postpartum depression was found in a study [49].

Social support: Receiving social support through friends and relatives during stressful times is thought to be a protective factor against developing depression [54] and several earlier studies have evaluated the role of social support in reducing postpartum depression.

20.7.2 Moderate Risk Factors

Psychological factors: Maternal personality characteristics including neuroticism and cognitive attributional style have been measured as risk factors for postpartum depression [49, 55].

Marital relationship: Studies have reported an increased risk of postpartum depression in women who experienced marital problems during pregnancy [49, 50, 56].

20.7.3 Minor Risk Factors

Obstetric factors: Obstetric factors including pregnancy-related complications have been examined as potential risk factors for postpartum depression [49, 53, 57, 58].

Socioeconomic status: Socioeconomic deprivation indicators such as unemployment, low income, and low education have been cited as risk factors in mental health disorders, and in depression in particular [59–61].

20.8 Effects of Illness

Postpartum depression has not only deleterious consequences for the mother but also for the baby and can delay the physical, social, and cognitive development of the baby. Therefore, it is very important to prevent this disease at the centers of women's care using a multidisciplinary approach.

The interaction disturbances of depressed mothers and their infants appear to be universal, across different cultures and socioeconomic status groups. All mothers have in common that they show less sensitivity to and responsibility for the infants [62].

Maternal depression can have a negative impact in different areas of the infants, a range of cognitive functions [63], and verbal abilities [64], as well as children's abilities to regulate their own emotions and behaviors [65]. Parenting can often be influenced by the effects of maternal depression; this may be caused by depressed mothers exhibiting decreased sensitivity in interactions with children, and the lack of contingency in response to the actions of child [66, 67].

Maternal depression is not the only factor that affects children's development; contextual risks can also have a negative impact on children's cognitive functioning, including executive functions such as attention [68], inhibitory control [69], IQ [70], and language development [71].

The possible impact of risks in the context of children's cognitive functioning may be higher in parents with a lower educational level and fewer resources to encourage them cognitively [72].

The interpersonal stress of depressed mothers can negatively affect the well-being of adolescents [73, 74] and children [75], considering that early in the life course, the mother constitutes the primary social environment for the child [76].

It is important to highlight the importance that the immediate social environment has for the baby and his/her experiences; the effect of both maternal depression and contextual risks on the children may be considerable [73]. However, postpartum depression also has important consequences for the mother. At this important moment of her life, she is supposed to meet certain expectations, and discomfort caused by not being able to do so is added to the discomfort of depression.

20.9 Effects on the Mother

Depression after childbirth affects the woman's feelings about herself and her interpersonal relationships. It is remarkable in the mother–baby relationship, the couple relationship, and relationships with older children and the wider family are influenced by the depression of the mother. It is important to note that women with postnatal depression are at an increased risk of future depressive episodes. In the postnatal period, an additional challenge for the mother is coping with depression at a time when there is a strong societal expectation that motherhood is joyful and rewarding [77, 78]. Thus, we must not forget that social expectations about motherhood can increase women's reluctance to disclose negative feelings.

20.10 Effects of Depression on the Child

There are many factors that contribute to the healthy development of the child, but development can also be disrupted by many factors. Early relationships are central in promoting healthy social and emotional child development [79]. Having a depressed mother has an impact on the cognitive development of the children, including language development and intelligence. All this varies with the child's gender, different social factors, and the timing and course of the mother's depression [80, 81]. It is obvious to think that the mother's ability to regulate her baby's state plays an important role in helping children develop strategies for managing their feelings and emotions [82, 83]. Some studies showed that mothers with postnatal depression display more negative behaviors toward their babies and that their babies are less positive than those of nondepressed mothers [82, 84].

20.11 Treatment

Nowadays, the idea that postpartum depression is similar to nonpuerperal depression has changed. Until recently, this idea was supported by most investigators and clinicians, but at present and because of the results of some studies that showed that sex steroids have pronounced effects on the central nervous system, including the areas responsible for mood and cognition, this idea has changed [85]. Furthermore, the observation that women become depressed at twice the rate of men and are particularly vulnerable at times of hormonal fluctuation suggests that depression

occurring at such times may be, in part, hormonally driven. Because of this association, several investigators have examined the role of estrogen in the treatment and prophylaxis of postpartum depression [25, 86].

In the meantime, the treatment of postpartum depression is based on that of nonpuerperal depression [87–89]. Psychotherapy or pharmacotherapy may be used alone or in combination. Because no modality has been shown to be superior to any other, some authors argue that the choice of therapy, pharmacological and/or psychotherapeutic, for mild to moderate postpartum depression, may be left to the patient [87].

20.12 Psychotherapy

Puerperal women may benefit from psychotherapy, as it focuses on the patient's interpersonal relationships and changing roles [90]. Although pharmacological treatment is also an option, because of the relative paucity of information about the safety of antidepressant use during breastfeeding, many women may choose a nonpharmacological treatment to avoid exposing the baby to psychotropic medication. Marriage counseling is warranted when marital conflicts are distressing and perhaps contribute to depression in women.

20.13 Antidepressant Therapy

Antidepressant treatment may be a suitable medication for any woman with postpartum depression, but especially in cases of persistent depression, or in women who have difficulties caring for themselves or who even have thoughts of harming themselves or the baby, antidepressant treatment has to be the therapy of choice after a comprehensive assessment of the case.

Besides antidepressants, a woman with postpartum depression may benefit from treatment with benzodiazepines to treat the anxiety and agitation that accompany depression. However, the use of antidepressants at this stage of life is something to be controlled, and many of the mothers take the option to breastfeed. In different reviews we have seen that the blood concentration of tricyclic and SSRI antidepressants have been below the detection limit of the laboratory [91]. However, the evidence shows that although well tolerated in the plasma of some babies, detectable levels of antidepressants were found, since these metabolites pass to the baby through breast milk [87, 92–96]. Thus, it is especially important to determine the duration of antidepressant treatment in lactating women [97].

20.14 Discussion

In the last few years this disorder has been considered a public health problem. The World Health Organization/United Nations Population Fund (WHO-UNFPA) [98] has identified maternal mental health as fundamental in achieving the Millennium Development Goals and the Marcé Society for Perinatal Mental Health [99] proposes a debate on the need for a universal psychosocial assessment and detection of depression in perinatal women in the field of primary health care.

Postnatal depression must be carefully distinguished from both normal and other postpartum psychiatric disorders common in this period, among which are dysphoria and postpartum psychosis. For this reason, it is important to have good screening tools to detect the possible presence of these symptoms in order to assess the severity and make a differential diagnosis.

The duration of postpartum depression is not equal in all cases. In some cases it is resolved within a few months of initiation; others, however, are extended in duration [56]. For many women, childbirth is the stress factor that has led them to trigger a series of recurrent depressive episodes that may become chronic. After an episode of postpartum depression the risk of recurrence is 25 %, i.e., they are likely to have more depressive episodes throughout their life, besides being more likely to have them in the postpartum period [56, 58, 100, 101].

It is important to educate about the risk factors for both healthcare professionals who have contact with the mother during pregnancy and the mother, as detecting these early can prevent her from developing depression. Practitioners have to be aware and education about the issue is of vital importance, for mothers not to confuse depression symptoms with pregnancy process symptoms.

Although the theory of hormonal changes in delivery is based on the influence of endocrine factors on the development of PND, there are contradictory findings in the literature so it is essential to continue researching new hypotheses about how the different causes such as psychosocial aspects and gender issues referred to in the previous chapter make some women more vulnerable to developing the disease.

Women in more vulnerable groups to which we must pay special attention include women with conflictive relationships, those who have suffered stressful life events, women of a lower socioeconomic level, as these women are, along with those with a lack of social support at a higher risk of developing postpartum depression.

Treatment of depressed women in the postpartum period may be different according to the characteristics of the case. In general, therapy may be beneficial for the symptoms, both individual and group therapy. Drug treatment is also a good option, especially in cases where postpartum depression is considered moderate or severe, where there are suicidal thoughts, or where it actually affected functionality in women in whom therapy was not effective. The use of tricyclic antidepressants and SSRIs are not contraindicated during lactation, but in cases that thrive and choose breastfeeding for the baby, taking antidepressants must be done with exhaustive control so that this does not affect the child, because the benefits of

taking an antidepressant are probably greater than the risk of psychotropic exposure of the child.

References

1. Burt VK, Stein K. Epidemiology of depression throughout the female life cycle. *J Clin Psychiatry*. 2002;63 Suppl 7:9–15.
2. Gaynes BN, Gavin N, Meltzer-Brody S, Lohr KN, Swinson T, Gartlehner G, et al. Perinatal depression: prevalence, screening accuracy, and screening outcomes. *Evid Rep Technol Assess (Summ)* 2005;(119):1–8.
3. MacArthur. Initiative on depression and primary care. Patient health questionnaire (PHQ-9). <http://depressionprimarycare.org/clinicians/toolkits/materials/forms/phq9>; 2010 April 10.
4. Bonari L, Pinto N, Ahn E, Einarson A, Steiner M, Koren G. Perinatal risks of untreated depression during pregnancy. *Can J Psychiatry*. 2004;49(11):726–35.
5. Kendell RE, McGuire RJ, Connor Y, Cox JL. Mood changes in the first three weeks after childbirth. *J Affect Disord*. 1981;3(4):317–26.
6. Sit D, Rothschild AJ, Wisner KL. A review of postpartum psychosis. *J Womens Health (Larchmt)*. 2006;15(4):352–68.
7. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed; 2013.
8. Wisner KL, Parry BL, Piontek CM. Clinical practice. Postpartum depression. *N Engl J Med*. 2002;347(3):194–9.
9. Not author listed. The management of postnatal depression. *Drug Ther Bull* 2000;38(5):33–7.
10. Gavin NI, Gaynes BN, Lohr KN, Meltzer-Brody S, Gartlehner G, Swinson T. Perinatal depression: a systematic review of prevalence and incidence. *Obstet Gynecol*. 2005;106 (5 Pt 1):1071–83.
11. Halbreich U, Karkun S. Cross-cultural and social diversity of prevalence of postpartum depression and depressive symptoms. *J Affect Disord*. 2006;91(2–3):97–111.
12. Affonso DD, De AK, Horowitz JA, Mayberry LJ. An international study exploring levels of postpartum depressive symptomatology. *J Psychosom Res*. 2000;49(3):207–16.
13. Brugha TS, Morrell CJ, Slade P, Walters SJ. Universal prevention of depression in women postnatally: cluster randomized trial evidence in primary care. *Psychol Med*. 2011;41 (4):739–48.
14. Dennis CL. Preventing and treating postnatal depression. *BMJ*. 2009;338:a2975.
15. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry*. 1987;150:782–6.
16. Buist AE, Barnett BE, Milgrom J, Pope S, Condon JT, Ellwood DA, et al. To screen or not to screen—that is the question in perinatal depression. *Med J Aust*. 2002;177(Suppl):S101–5.
17. Lanes A, Kuk JL, Tamim H. Prevalence and characteristics of postpartum depression symptomatology among Canadian women: a cross-sectional study. *BMC Public Health*. 2011;11:302.
18. Georgiopoulos AM, Bryan TL, Wollan P, Yawn BP. Routine screening for postpartum depression. *J Fam Pract*. 2001;50(2):117–22.
19. Dorr HG, Heller A, Versmold HT, Sippell WG, Herrmann M, Bidlingmaier F, et al. Longitudinal study of progestins, mineralocorticoids, and glucocorticoids throughout human pregnancy. *J Clin Endocrinol Metab*. 1989;68(5):863–8.
20. Stalla GK, Bost H, Stalla J, Kaliebe T, Dorr HG, Pfeiffer D, et al. Human corticotropin-releasing hormone during pregnancy. *Gynecol Endocrinol*. 1989;3(1):1–10.
21. Bloch M, Daly RC, Rubinow DR. Endocrine factors in the etiology of postpartum depression. *Compr Psychiatry*. 2003;44(3):234–46.

22. Skalkidou A, Hellgren C, Comasco E, Sylven S, Sundstrom PI. Biological aspects of postpartum depression. *Womens Health (Lond Engl)*. 2012;8(6):659–72.
23. Bloch M, Schmidt PJ, Danaceau M, Murphy J, Nieman L, Rubinow DR. Effects of gonadal steroids in women with a history of postpartum depression. *Am J Psychiatry*. 2000;157(6):924–30.
24. Ahokas A, Kaukoranta J, Wahlbeck K, Aito M. Estrogen deficiency in severe postpartum depression: successful treatment with sublingual physiologic 17beta-estradiol: a preliminary study. *J Clin Psychiatry*. 2001;62(5):332–6.
25. Gregoire AJ, Kumar R, Everitt B, Henderson AF, Studd JW. Transdermal oestrogen for treatment of severe postnatal depression. *Lancet*. 1996;347(9006):930–3.
26. Klier CM, Muzik M, Dervic K, Mossaheb N, Benesch T, Ulm B, et al. The role of estrogen and progesterone in depression after birth. *J Psychiatr Res*. 2007;41(3–4):273–9.
27. Harris B, Lovett L, Newcombe RG, Read GF, Walker R, Riad-Fahmy D. Maternity blues and major endocrine changes: Cardiff puerperal mood and hormone study II. *BMJ*. 1994;308(6934):949–53.
28. Nappi RE, Petraglia F, Luisi S, Polatti F, Farina C, Genazzani AR. Serum allopregnanolone in women with postpartum “blues”. *Obstet Gynecol*. 2001;97(1):77–80.
29. Harris B, Lovett L, Smith J, Read G, Walker R, Newcombe R. Cardiff puerperal mood and hormone study. III. Postnatal depression at 5 to 6 weeks postpartum, and its hormonal correlates across the peripartum period. *Br J Psychiatry*. 1996;168(6):739–44.
30. Bou-Saleh MT, Ghubash R, Karim L, Krymski M, Bhai I. Hormonal aspects of postpartum depression. *Psychoneuroendocrinology*. 1998;23(5):465–75.
31. Lawrie TA, Hofmeyr GJ, De JM, Berk M, Paiker J, Viljoen E. A double-blind randomised placebo controlled trial of postnatal norethisterone enanthate: the effect on postnatal depression and serum hormones. *Br J Obstet Gynaecol*. 1998;105(10):1082–90.
32. Chrousos GP, Gold PW. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *JAMA*. 1992;267(9):1244–52.
33. Kammerer M, Taylor A, Glover V. The HPA axis and perinatal depression: a hypothesis. *Arch Womens Ment Health*. 2006;9(4):187–96.
34. Jolley SN, Elmore S, Barnard KE, Carr DB. Dysregulation of the hypothalamic-pituitary-adrenal axis in postpartum depression. *Biol Res Nurs*. 2007;8(3):210–22.
35. Taylor A, Glover V, Marks M, Kammerer M. Diurnal pattern of cortisol output in postnatal depression. *Psychoneuroendocrinology*. 2009;34(8):1184–8.
36. Corwin EJ, Pajer K. The psychoneuroimmunology of postpartum depression. *J Womens Health (Larchmt)*. 2008;17(9):1529–34.
37. Maes M, Yirmiya R, Noraberg J, Brene S, Hibbeln J, Perini G, et al. The inflammatory and neurodegenerative (I&ND) hypothesis of depression: leads for future research and new drug developments in depression. *Metab Brain Dis*. 2009;24(1):27–53.
38. Raison CL, Capuron L, Miller AH. Cytokines sing the blues: inflammation and the pathogenesis of depression. *Trends Immunol*. 2006;27(1):24–31.
39. Pter-Levy Y, Feldman M, Vakart A, Ebstein RP, Feldman R. Impact of maternal depression across the first 6 years of life on the child’s mental health, social engagement, and empathy: the moderating role of oxytocin. *Am J Psychiatry*. 2013;170(10):1161–8.
40. Viero C, Shibuya I, Kitamura N, Verkhratsky A, Fujihara H, Katoh A, et al. Review: oxytocin: Crossing the bridge between basic science and pharmacotherapy. *CNS Neurosci Ther*. 2010;16(5):e138–56.
41. Feldman R. Oxytocin and social affiliation in humans. *Horm Behav*. 2012;61(3):380–91.
42. Basraon S, Costantine MM. Mood disorders in pregnant women with thyroid dysfunction. *Clin Obstet Gynecol*. 2011;54(3):506–14.
43. Kuijpers JL, Vader HL, Drexhage HA, Wiersinga WM, van Son MJ, Pop VJ. Thyroid peroxidase antibodies during gestation are a marker for subsequent depression postpartum. *Eur J Endocrinol*. 2001;145(5):579–84.

44. De CF, Perelli F, Armando M, Vicari S. Selective serotonin reuptake inhibitors (SSRIs) for post-partum depression (PPD): a systematic review of randomized clinical trials. *J Affect Disord.* 2014;152–154:39–44.
45. Anderson G, Maes M. Postpartum depression: psychoneuroimmunological underpinnings and treatment. *Neuropsychiatr Dis Treat.* 2013;9:277–87.
46. Pawlby S, Hay DF, Sharp D, Waters CS, O’Keane V. Antenatal depression predicts depression in adolescent offspring: prospective longitudinal community-based study. *J Affect Disord.* 2009;113(3):236–43.
47. Mehta D, Quast C, Fasching PA, Seifert A, Voigt F, Beckmann MW, et al. The 5-HTTLPR polymorphism modulates the influence on environmental stressors on peripartum depression symptoms. *J Affect Disord.* 2012;136(3):1192–7.
48. Mitchell C, Notterman D, Brooks-Gunn J, Hobcraft J, Garfinkel I, Jaeger K, et al. Role of mother’s genes and environment in postpartum depression. *Proc Natl Acad Sci USA.* 2011;108(20):8189–93.
49. O’Hara MW, Swain AM. Rates and risk of postpartum depression—a meta-analysis. *Int Rev Psychiatry.* 1996;8:37–54.
50. Beck CT. Predictors of postpartum depression: an update. *Nurs Res.* 2001;50(5):275–85.
51. Josefsson A, Angelsioo L, Berg G, Ekstrom CM, Gunnervik C, Nordin C, et al. Obstetric, somatic, and demographic risk factors for postpartum depressive symptoms. *Obstet Gynecol.* 2002;99(2):223–8.
52. Neter E, Collins NL, Lobel M, Dunkel-Schetter C. Psychosocial predictors of postpartum depressed mood in socioeconomically disadvantaged women. *Womens Health.* 1995;1(1):51–75.
53. Johnstone SJ, Boyce PM, Hickey AR, Morris-Yatees AD, Harris MG. Obstetric risk factors for postnatal depression in urban and rural community samples. *Aust N Z J Psychiatry.* 2001;35(1):69–74.
54. Brugha TS, Sharp HM, Cooper SA, Weisender C, Britto D, Shinkwin R, et al. The Leicester 500 Project. Social support and the development of postnatal depressive symptoms, a prospective cohort survey. *Psychol Med.* 1998;28(1):63–79.
55. Lee DT, Yip AS, Leung TY, Chung TK. Identifying women at risk of postnatal depression: prospective longitudinal study. *Hong Kong Med J.* 2000;6(4):349–54.
56. Kumar R, Robson KM. A prospective study of emotional disorders in childbearing women. *Br J Psychiatry.* 1984;144:35–47.
57. Nielsen FD, Videbech P, Hedegaard M, Dalby SJ, Secher NJ. Postpartum depression: identification of women at risk. *BJOG.* 2000;107(10):1210–7.
58. Warner R, Appleby L, Whitton A, Faragher B. Demographic and obstetric risk factors for postnatal psychiatric morbidity. *Br J Psychiatry.* 1996;168(5):607–11.
59. Bartley M. Unemployment and ill health: understanding the relationship. *J Epidemiol Community Health.* 1994;48:333–7.
60. Patel V, Araya R, de Lima M, Ludermir A, Todd C. Women, poverty and common mental disorders in four restructuring societies. *Soc Sci Med.* 1999;49(11):1461–71.
61. World Health Organization. The World Health Report 2001: determinants of mental and behavioural disorders. Web Site World Health Organization 2001.
62. Field T. Postpartum depression effects on early interactions, parenting, and safety practices: a review. *Infant Behav Dev.* 2010;33(1):1–6.
63. Hughes C, Roman G, Hart MJ, Ensor R. Does maternal depression predict young children’s executive function?—a 4-year longitudinal study. *J Child Psychol Psychiatry.* 2013;54(2):169–77.
64. Barker ED, Jaffee SR, Uher R, Maughan B. The contribution of prenatal and postnatal maternal anxiety and depression to child maladjustment. *Depress Anxiety.* 2011;28(8):696–702.

65. Feldman R, Eidelman AI. Biological and environmental initial conditions shape the trajectories of cognitive and social-emotional development across the first years of life. *Dev Sci*. 2009;12(1):194–200.
66. Cox AD, Puckering C, Pound A, Mills M. The impact of maternal depression in young children. *J Child Psychol Psychiatry*. 1987;28(6):917–28.
67. Hay DF, Pawlby S, Sharp D, Asten P, Mills A, Kumar R. Intellectual problems shown by 11-year-old children whose mothers had postnatal depression. *J Child Psychol Psychiatry*. 2001;42(7):871–89.
68. Rueda MR, Posner MI, Rothbart MK. The development of executive attention: contributions to the emergence of self-regulation. *Dev Neuropsychol*. 2005;28(2):573–94.
69. Farah MJ, Shera DM, Savage JH, Betancourt L, Giannetta JM, Brodsky NL, et al. Childhood poverty: specific associations with neurocognitive development. *Brain Res*. 2006;1110(1):166–74.
70. Duncan GJ, Brooks-Gunn J. Family poverty, welfare reform, and child development. *Child Dev*. 2000;71(1):188–96.
71. Noble KG, McCandliss BD, Farah MJ. Socioeconomic gradients predict individual differences in neurocognitive abilities. *Dev Sci*. 2007;10(4):464–80.
72. Conger RD, Donnellan MB. An interactionist perspective on the socioeconomic context of human development. *Annu Rev Psychol*. 2007;58:175–99.
73. Garber J, Cole DA. Intergenerational transmission of depression: a launch and grow model of change across adolescence. *Dev Psychopathol*. 2010;22(4):819–30.
74. Hammen C, Shih JH, Brennan PA. Intergenerational transmission of depression: test of an interpersonal stress model in a community sample. *J Consult Clin Psychol*. 2004;72(3):511–22.
75. Barker ED. The duration and timing of maternal depression as a moderator of the relationship between dependent interpersonal stress, contextual risk and early child dysregulation. *Psychol Med*. 2013;43(8):1587–96.
76. Murray L, Kempton C, Woolgar M, Hooper R. Depressed mothers' speech to their infants and its relation to infant gender and cognitive development. *J Child Psychol Psychiatry*. 1993;34(7):1083–101.
77. Hall PL, Wittkowski A. An exploration of negative thoughts as a normal phenomenon after childbirth. *J Midwifery Womens Health*. 2006;51(5):321–30.
78. Petch J, Halford WK. Psycho-education to enhance couples' transition to parenthood. *Clin Psychol Rev*. 2008;28(7):1125–37.
79. Thompson RA. Early sociopersonality development. In: Damon WE, editor. *Handbook of child psychology, Social, emotional and personality development*, vol. 3. 5th ed. New York: Wiley; 1998. p. 25–104.
80. Grace SL, Evindar A, Stewart DE. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature. *Arch Womens Ment Health*. 2003;6(4):263–74.
81. Hay DF, Pawlby S, Angold A, Harold GT, Sharp D. Pathways to violence in the children of mothers who were depressed postpartum. *Dev Psychol*. 2003;39(6):1083–94.
82. Hay DF. Postpartum depression and cognitive development. In: Cooper P, Murray L, editors. *Postpartum depression and child development*. New York: Guilford; 1997. p. 85–110.
83. Tronick E, Reck C. Infants of depressed mothers. *Harv Rev Psychiatry*. 2009;17(2):147–56.
84. Murray L, Cooper P. Effects of postnatal depression on infant development. *Arch Dis Child*. 1997;77(2):99–101.
85. Boyce P, Stubbs J, Todd A. The Edinburgh Postnatal Depression Scale: validation for an Australian sample. *Aust N Z J Psychiatry*. 1993;27(3):472–6.
86. Sichel DA, Cohen LS, Robertson LM, Ruttenberg A, Rosenbaum JF. Prophylactic estrogen in recurrent postpartum affective disorder. *Biol Psychiatry*. 1995;38(12):814–8.

87. Appleby L, Warner R, Whitton A, Faragher B. A controlled study of fluoxetine and cognitive-behavioural counselling in the treatment of postnatal depression. *BMJ*. 1997;314(7085):932–6.
88. Stowe ZNCJLJNC, Casarella J, Landry J, Nemeroff CB. Sertraline in the treatment of women with postpartum major depression. *Depression*. 1995;3:49–55.
89. Epperson CN, McDougle CJ, Ward-O'Brien D, Price LH. A controlled study of sertraline versus placebo in the treatment of postpartum depression: preliminary findings. *Soc Neurosci*. 1996;22:179. Ref Type: Abstract.
90. Stuart SOM, O'Hara MW. Treatment of postpartum depression with interpersonal psychotherapy [Letter]. *Arch Gen Psychiatry*. 1995;52:75–6.
91. Wisner KL, Perel JM, Findling RL. Antidepressant treatment during breast-feeding. *Am J Psychiatry*. 1996;153(9):1132–7.
92. Epperson CN, Anderson GM, McDougle CJ. Sertraline and breast-feeding. *N Engl J Med*. 1997;336(16):1189–90.
93. Lester BM, Cucca J, Andreozzi L, Flanagan P, Oh W. Possible association between fluoxetine hydrochloride and colic in an infant. *J Am Acad Child Adolesc Psychiatry*. 1993;32(6):1253–5.
94. Spigset O, Carleborg L, Norstrom A, Sandlund M. Paroxetine level in breast milk. *J Clin Psychiatry*. 1996;57(1):39.
95. Wisner KL, Perel JM, Findling RL, Hinnes RL. Nortriptyline and its hydroxymetabolites in breastfeeding mothers and newborns. *Psychopharmacol Bull*. 1997;33(2):249–51.
96. Wright S, Dawling S, Ashford JJ. Excretion of fluvoxamine in breast milk. *Br J Clin Pharmacol*. 1991;31(2):209.
97. American Academy of Pediatrics Work Group on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics*. 1997;100:1035–9.
98. WHO-UNFPA. The Millennium Development Goals Report 2012. <https://www.unfpa.org/public/publications/pid/6090>; 2013
99. Marcé International Society. <http://www.marcesociety.com/About-Marce.aspx>; 2013. Ref Type: Internet Communication.
100. Nott PN. Extent, timing and persistence of emotional disorders following childbirth. *Br J Psychiatry*. 1987;151:523–7.
101. Philipps LH, O'Hara MW. Prospective study of postpartum depression: 4 1/2-year follow-up of women and children. *J Abnorm Psychol*. 1991;100(2):151–5.