

Hormonal conditions of postpartum depression

Hormonalne uwarunkowania depresji poporodowej

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KEYWORDS:

- postpartum depression
- pregnancy
- hormonal disturbances in pregnancy
- hormonal changes after delivery

ABSTRACT

The sudden drop in the level of postpartum certain hormones, especially estrogens and progesterone, promotes mood disorders. Some women may have severe symptoms of postpartum depression, that need timely diagnosis and proper treatment. Women with premenstrual syndrome symptoms are particularly at risk of depression.

To prevent the dangerous consequences of unrecognized postpartum depression, a requirement was introduced in 2019 in Poland for gynecologists to interview pregnant women and to exclude the occurrence of depression in the postpartum period.

The aim of the study is to present the hormonal determinants of postpartum depression with particular attention to risk factors.

SŁOWA KLUCZOWE:

- depresja poporodowa
- ciąża
- zmiany hormonalne w ciąży
- zaburzenia hormonalne po porodzie

STRESZCZENIE

Nagły spadek stężenia niektórych hormonów po porodzie, zwłaszcza estrogenów i progesteronu, sprzyja zaburzeniom nastroju. Niektóre kobiety mogą mieć poważne objawy depresji poporodowej, które wymagają szybkiej diagnozy i odpowiedniego leczenia. Szczególnie narażone na depresję poporodową są kobiety z objawami zespołu napięcia przedmiesiączkowego występującymi przed ciążą.

Aby zapobiec niebezpiecznym konsekwencjom nierozpoznanej depresji poporodowej, w 2019 roku wprowadzono w Polsce wymóg przeprowadzania testów u kobiet w ciąży i po porodzie, aby wykluczyć występowanie u nich depresji.

Celem pracy jest przedstawienie hormonalnych uwarunkowań depresji poporodowej ze szczególnym zwróceniem uwagi na czynniki ryzyka.

Introduction

Postpartum depression – definition and epidemiology

Peripartum depression is defined as an episode of major depressive disorder (MDD) occurring during pregnancy and within 4 weeks of delivery (1). Some authors question the above time criteria as too narrow (2), rather proposing a period of 12 months after delivery.

According to the World Health Organization (WHO), the perinatal period is defined as the period of pregnancy and 6 weeks after delivery. It is a collective definition covering the periods proposed by WHO (3) and the Diagnostic and Statistical Manual of Mental Disorders (DSM) (DSM-5, 2013). The perinatal period is a time of increased susceptibility to an affective episode, which is associated with shallow but short-term fluctuations in sex hormone levels in pregnancy, and intensified in the postpartum period (4, 5). The occurrence of depression in the perinatal period is most likely genetically determined. The heritability of perinatal depression was

estimated at 54% and 44%, respectively, in separate samples, and the heritability of nonperinatal depression at 32% (6). Candidate gene studies have largely focused on genes previously implicated in major depressive disorder, such as the serotonin transporter, tryptophan hydroxylase-2 (TPH2), Catechol-O-methyl transferase (COMT), Monoamine Oxidase (MAO), and Brain Derived Neurotrophic Factor (BDNF) (7).

Antenatal and postnatal depression are often collectively combined as maternal depression, since depressive symptoms during lactation may begin de novo or be a continuation of depression already present during pregnancy. Up to 20% of women reveal symptoms of postpartum depression within 30 days of delivery (8, 9), but an increased risk of mood disorders persists for up to 2 years.

Incidence

It is assumed that postpartum depression occurs with a frequency of about 12% (compared with 16% during pregnancy) (10),

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although the frequency rates vary depending on the diagnostic criteria used for depression and the method of its diagnosis (11, 12). Antenatal and postpartum depression are more common in countries with a low birth rate (25.3% in total) (12). According to some studies, up to 50% of postpartum depression cases remain undiagnosed (13, 14), one of the reasons for this is that mothers hide their symptoms.

Diagnosis of postpartum depression

As with other disorders, the diagnosis of postpartum depression is made using the diagnostic criteria of large disease classification systems: ICD-10 and DSM-5. In the ICD-10 classification, the time frame for the diagnosis of puerperium disorders is 6 weeks from delivery. The classification divides these disorders into mild (F 53.0) and severe (F 53.1). The criterion of severity is the occurrence of psychotic symptoms.

In the absence of biological markers, psychopathological scales are used to increase the accuracy of the diagnosis. The analysis of research on postnatal depression originating in the USA makes it possible to find many scales used to diagnose depression. In a recent review (15), 23 articles on postnatal symptoms in the US population used 17 self-assessment scales of depression, along with a diet (ESI) and physical activity (MAQ) assessment questionnaire. There are scales dedicated to postpartum depression: Postpartum Depression Screening Scale (PDSS), Edinburgh Postpartum Depression Scale (EPDS), Corea-Barrick Postpartum Depression Scale (CBPDS), Pregnancy Risk Assessment Monitoring System (PRAMS); classic scales of general depression assessment: Beck Depression Inventory (BDI), Hamilton Rating Scale for Depression (HRDS), and Center for Epidemiologic Studies Depression Scale (CES-D); as well as scales of overall health assessment: Patient Health Questionnaire (PHQ), Structured Clinical Interviews for DSM Disorders (SCID for DSM-5). One of the scales concerns the symptoms of psychological distress with depression as the main component (PDM, Postpartum Distress Measure). The length of postnatal assessment scales is most often significant (e.g., PDSS: 35 items, EPDS: 10 items), hence, some of the postpartum depression assessment scales have shortened versions of 2-7 items (PDSS-SF, EPDS-2/EPDS-7, PRAMS-3D).

However, the classic scales of Hamilton Depression Rating Scale (HAMD) completed by a doctor, and the Beck Depression self-report Inventory (BDI) are considered the gold standard in the diagnosis of depression. The tool dedicated to the diagnosis of perinatal depression and the most widely used for this purpose is the EPDS. The EPDS scale is a short self-assessment scale used in screening for depression during pregnancy and after delivery. A score of ≥ 10 or sometimes ≥ 13 suggests the presence of perinatal depression requiring a more detailed clinical assessment (16). So far, there is no research on the use of the EPDS scale in postpartum women with severe depression. In this study, the reliability ratios (mainly alpha internal consistency coefficients) for all scales were over 0.8, and the accuracy indicators (usually expressed as Pearson's correlation coefficients) were over 0.7. However, high rates of sensitivity (70%) and specificity (90%) were shown only for the EPDS scale (16). The need for tools to assess specific problems has been underlined in recent years. Great importance in postpartum depression is attributed to screening, enabling early intervention and better treatment results (18). In the past,

the optimal period for screening was thought to be quite wide, ranging from 2 to 24 weeks after delivery (19). Currently, some organizations, including the American College of Obstetricians and Gynecologists (ACOG) and the National Institute for Health and Clinical Excellence (NICE), recommend that depression self-assessment screening should be performed on every woman during postpartum follow-up visits (1, 3).

Hormonal changes during the physiological menstrual cycle

A characteristic feature of the hypothalamus-pituitary-ovary system in mature women is its cyclical function, manifest by periodic changes in the reproductive organ, referred to as the menstrual or sex cycle. The purpose of these changes is to prepare the woman's body for pregnancy. Two phases are distinguished in the physiological menstrual cycle: follicular and luteal (19).

In the first phase of the cycle – the follicular phase, after menstruation, estrogen concentration is very low. The estradiol (E2) concentration on the third day of the cycle is about 20-40 pg/mL (20). Due to the low level of estrogen in the blood, there is a change in the secretion of gonadotropin-releasing hormone (GnRH) by the hypothalamus wherein the frequency and the amplitude of its secretion increases, which causes a gradual increase in the secretion of follicle-stimulating hormone (FSH) by the pituitary gland. High levels of FSH and estradiol induce luteinizing hormone (LH) and progesterone receptor expression on luteal cells. The estradiol concentration is the highest just before the ovulation peak and amounts to about 200-350 pg/mL. Theca cells, under the influence of LH, produce androgens: androstenedione and testosterone. The granulosa cells of preovulatory follicles, that is, before the peak of LH secretion, express aromatase and 3β -hydroxysteroid dehydrogenase. An increase in GnRH secretion amplitude and frequency causes a LH peak. The ovulation peak of gonadotropin secretion causes ovulation, that is, the release of an egg from the follicle. The rupture of the Graafian follicle leads to the formation of the corpus luteum, which produces progesterone and other hormones needed to support pregnancy: estradiol, androgens, and protein hormones (21).

The increasing levels of estradiol and progesterone produce a number of changes: the thickening of the endometrium and development of vascularization during the proliferative phase in the uterus, in the cervical mucus, in the mammary glands (dilatation of the milk ducts and swelling of the breasts); as well as in the brain. Progesterone has a thermogenic effect and an increase in the basal body temperature of 0.4°C to 0.8°C is observed in the luteal phase.

The immune tolerance state is necessary for successful embryo implantation as, from an immunological point of view, the embryo is an antigenetically foreign body. Progesterone, like any steroid hormone, works immunosuppressively. The immune system must be "tuned" to allow for the implantation of the embryo in the uterine cavity, which involves a change the balance of Th1/Th2 lymphocytes. A disorder of this mechanism can result in early miscarriage.

If fertilization does not occur, the corpus luteum degenerates. The concentration of estrogen and progesterone gradually decreases, the endometrium is sloughed off, and menstruation occurs (19, 20).

Mood changes in the physiological menstrual cycle

In the first phase of the cycle, a woman is full of vigor, copes not only with personal duties but also with difficulties and adversities more easily; is more optimistic and, for instance, sportswomen perform better, and female students get better grades (21).

In the second phase of the cycle, a woman may be less fit, finds it more difficult to deal with her duties, and can be depressed and anxious. A woman also has larger and more sensitive breasts as the body retains more fluid during this time. These changes in appearance in the form of bloating and breast tenderness, for instance, are sometimes difficult for a woman to accept.

Hormonal changes in a physiological pregnancy

If fertilization occurs, the gestational corpus luteum develops. The trophoblast of the developing blastocyst produces chorionic gonadotropin (hCG), which acts on the same receptor as LH and prolongs the functioning of the corpus luteum. From 10-12 weeks of pregnancy, the role of the corpus luteum is taken over by the placenta and this becomes the real hormone factory (22). Never in their life are women exposed to such high levels of hormones as they are during pregnancy (23).

After giving birth, the woman is suddenly deprived of numerous hormones. Evidence that a subgroup of women are vulnerable to perinatal changes in reproductive hormones comes from treatment studies examining the effects of administering exogenous estradiol to women at high risk for PPD or those with active PPD symptoms (24). Some have hypothesized that the source of PPD vulnerability is in abnormal neural responses to the normal perinatal fluctuations in reproductive hormones. PPD is characterized by abnormal activation of the same brain regions implicated in non-puerperal major depression: the amygdala, insula, striatum, orbitofrontal cortex, and dorsomedial prefrontal cortex (25).

Perinatal and postpartum hormonal changes

The placenta is a unique organ that separates and, at the same time, connects the body of the mother and the fetus. The placenta produces a whole series of hormones: gonadoliberin (stimulating hCG secretion), chorionic gonadotropin (stimulating the secretion of estrogens and progesterone), thyroliberin, corticoliberin, gonadoliberin, somatostatin, somatoliberin, adrenocorticotropin, and many other neurohormones (β -endorphins, neuropeptide Y). It also produces growth factors: insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), and fibroblast growth factor (FGF) (21).

Progesterone – the main pregnancy hormone

Progesterone is made from pregnenolone, which comes from cholesterol. Production takes place in the mother's adrenal glands and in the placenta. Progesterone levels depend on the week of pregnancy. At the end of pregnancy, a pregnant woman produces approximately 300 mg of progesterone per day. The highest progesterone concentration is observed in the antenatal period (approx. 200 ng/mL).

Estrogens in pregnancy

Estrogen hormones: estradiol, estrone, and estriol, are produced during pregnancy.

Estradiol is the strongest estrogen, its concentration at the end of pregnancy is 50-100 times higher than in the menstrual cycle. Estrone is 10 times weaker than estradiol, its concentration increases several dozen times and is the highest just before delivery. Estriol is 100 times weaker than estradiol, at the end of pregnancy its concentration increases by about 1,000 times.

Placental estrogens are formed from dehydroepiandrosterone sulfate (DHEA-S). This hormone is produced by the placenta, as well as by the fetal and maternal adrenal glands, with the fetal adrenal glands producing about 10 times more. DHEA-S is then transformed by enzymes, but this process only occurs in the adrenals and fetal liver.

Prolactin in pregnancy

Prolactin is produced by the placental membranes but also secreted by the maternal pituitary gland and the fetal pituitary gland (21). Prolactin concentration is the highest shortly before delivery and is around 200 ng/mL.

Perinatal hormones

Just before delivery, the fetal adrenal glands produce large amounts of dehydroepiandrosterone sulfate, which is metabolized to estrogen. Fetal adrenals accelerate their growth from the 20th week of pregnancy and reach maximum dimensions 4 weeks before delivery. The highest increases of up to 5 times in DHEA-S and estrone levels occur in the last four days of pregnancy.

The placenta is the main site of progesterone production. Progesterone levels decline in the period preceding delivery. It is believed that the changing ratio of progesterone to estrogen in the fetal membranes is the mechanism that triggers labor.

Estriol (E3) is the estrogen whose concentration is the highest at the end of pregnancy. Its maximum concentration is observed during delivery. Increasing the estriol/estradiol ratio above 10:1 leads to the initiation of labor. Changes in the E3/E2 ratio in the blood and amniotic fluid do not reflect the situation in myometrium, where this ratio can be 700:1.

The secretion of estrogen is accelerated by corticotropin-releasing hormone (CRH) secreted by the maternal pituitary gland, the fetus pituitary gland, and the placenta. During pregnancy, CRH production is inhibited by progesterone. The concentration of progesterone decreases and the concentration of CRH increases before delivery, which stimulates the secretion of adrenocorticotrophic hormone (ACTH) and the production of DHEA-S and estrogens.

An increase in the fetal CRH concentration precedes the induction of surfactant protein synthesis in the maturing lungs. The rapid increase in the levels of CRH may signal that the fetus is ready to initiate labor (22).

Oxytocin is produced by the supraoptic and periventricular nuclei in the hypothalamus and secreted by the posterior pituitary lobe. It promotes the onset of labor by stimulating uterine contractions. Estrogens prepare the environment for oxytocin by creating oxytocin receptors. The fetus, as a source of estrogen precursors, affects the density of oxytocin receptors, thereby modulating uterine contractions.

Lactation

The mammary glands, under the influence of sex hormones, undergo reconstruction throughout pregnancy so that lactation is possible after delivery. Milk secretion begins after delivery once the estrogen and progesterone levels fall, which previously inhibited prolactin secretion. In the physiological menstrual cycle, prolactin concentration is about 20 ng/mL. Prolactin concentration increases during pregnancy and is about 140 ng/mL in the perinatal period. In addition, stimulating the nipple (newborn suckling) increases prolactin production. In lactating women, prolactin levels are elevated throughout lactation (20, 22).

Changes to mood after birth

Mood changes after delivery were first described in 1858. It is estimated that postpartum depression occurs in about 8% of postpartum women up to 6 weeks after delivery, and in 14% of women up to 12 weeks after delivery. The symptoms of depression usually appear within the first two weeks of delivery (22).

After delivery, many hormones drop suddenly and dramatically. The delivery of the baby and the placenta causes a sharp decrease in the levels of progesterone, estrogens, cortisol, thyroid hormones, as well as β -endorphins, and hCG.

Thyroxine and triiodothyronine levels also decrease after delivery, which reduces serotonin levels, triggering mood disorders. The presence of thyroid antibodies additionally promotes postpartum depression. Mood disorders are more common in women with Hashimoto's disease compared to women with no autoimmune disease.

Female sex hormones are known to affect neuronal function: estrogens increase neuronal excitability

by stimulating glutamate receptors, while progesterone and its metabolites, mainly allopregnanolone, exert an inhibitory effect through postsynaptic γ -aminobutyric acid (GABA) receptors. Allopregnanolone has antidepressant, sedative, and anticonvulsant effects.

Progesterone is synthesized in the nervous system de novo from cholesterol, and its synthesis in the nervous system occurs independently of the synthesis in the endocrine glands. It has been demonstrated that progesterone concentrations in the brain tissue of male and female rats did not change after adrenalectomy and castration.

As **estradiol** also increases allopregnanolone, a decrease in post-delivery estradiol may further cause fluctuations in allopregnanolone, resulting in GABA receptor dysregulation. This, in turn, can also cause the dysregulation of the hypothalamic-pituitary-adrenal axis, resulting in an increased vulnerability to depression.

However, postpartum depressive symptoms are thought to be mainly caused by progesterone deficiency. Progesterone in the nervous system, regardless of its origin (hormone, neurosteroid), exerts neurotrophic and neuroprotective effects. It also stimulates myelination and remyelination in the central (oligodendrocytes) and peripheral (Schwann cells) nervous system.

Allopregnanolone is synthesized from progesterone. It is a neurosteroid that has been shown to have antidepressant effects (22). Its amount decreases abruptly after delivery, which can lead to brain changes responsible for depression and anxiety disorders. The discovery of this effect led to the approval by the Food and Drug Administration (FDA) of allopregnanolone for the treatment of postpartum depression. Brexanol is a synthetic type of allopregnanolone steroid administered as a continuous intravenous infusion over 60 hours in patients with postpartum depression.

Tab. 1. Hormone concentration of some steroids in the follicle phase and in the 40. week of pregnancy

Steroid	Follicle Phase	40. Week of pregnancy
Estradiol	0,05 ng/ml	20 ng/ml
Estriol	0,01 ng/ml	12 ng/ml
Progesteron	0,1 ng/ml	140 ng/ml
20 α -Dihydroprogesteron	0,2 ng/ml	25 ng/ml
5-Pregnenolon	0,1 ng/ml	8 ng/ml
5-Pregnenolonsulfat	2 ng/ml	400 ng/ml
Cortisol	100 ng/ml	150 ng/ml
Corticosteron	2 ng/ml	15 ng/ml
11-Deoxycorticosteron (DOC)	0,6 ng/ml	0,2 ng/ml
Pregnanolon	0,1 ng/ml	14 ng/ml
Testosteron	0,4 ng/ml	1,5 ng/ml
Dihydrotestosteron	0,2 ng/ml	0,2 ng/ml
Androstendion	1,5 ng/ml	3 ng/ml
DHEA	4 ng/ml	4 ng/ml
DHEA-Sulfat	3000 ng/ml	800 ng/ml

Postpartum depression – pathogenesis

The hypothalamic-pituitary-adrenal axis (HPA)

There is a plethora of inconsistent data generally confirming the importance of HPA axis activity in the development of postpartum depression. Some studies have shown elevated serum cortisol levels in women with postpartum depression, while others have not confirmed this, and others still have even shown an increase in mood associated with increased cortisol levels (28).

Abnormal HPA axis activity was often found in the course of major depression outside of pregnancy and postpartum, and was associated with higher initial levels of stress hormones, a more intense hormonal response to stress factors, and a decrease in the sensitivity of negative feedback loops expressed by the weakening of HPA axis inhibition in the dexamethasone test (29). Increased neurohormone (especially CRH) levels in cerebrospinal fluid, as well as increased CRH mRNA in the hypothalamus (in post-mortem studies) have been shown in patients with depression. CSF concentrations in the cerebrospinal fluid tended to normalize in the course of effective antidepressant treatment. It is known, however, that HPA axis function in patients with depression varies depending on its clinical picture (melancholic, agitated, anesthetic), therefore, these results may be distorted by the excessive heterogeneity across the studied groups.

In studies of patients with other types of depression (except during pregnancy and the puerperium), attention was paid to the importance of the course of the early mother-child relationship and the stress factors present in early childhood as a factor determining the constant increase in serum cortisol concentration. A hypothalamic-pituitary-adrenal axis dysfunction may be the cause of brain serotonergic regulation disorders (29, 30).

Brain serotonergic dysfunction

The activation of brain serotonergic pathways has been demonstrated in the course of postpartum depression (32). To examine potential alterations in serotonin signaling associated with postpartum depression, Moses-Kolko et al. (33) examined 5HT_{1A} binding potential using the ligand, [¹¹C]WAY100635. Binding at 5HT_{1A} receptors was significantly reduced in women with postpartum depression compared to healthy controls.

Differences in the levels of tryptophan, a serotonin precursor, have been shown in the perinatal period (34). One recent study using functional magnetic resonance imaging (fMRI) presented a different activation profile of the serotonergic areas of the brain in young mothers with depression, and without depression in response to their newborn crying (35). It has been suggested that genetic polymorphisms of the 5-HTT serotonin transporter are responsible for depression during pregnancy and after delivery (36).

Vitamin D deficiency and postpartum depression

It is widely believed that vitamin D₃ exerts a positive impact on the severity of depressive symptoms in adults as it has a pleiotropic effect in the central nervous system (37), and receptors for vitamin D are widespread in the human

brain (38). It has been postulated that vitamin D₃ modulates the levels of intraneuronal calcium ions, and vitamin D deficiency leads to an increase in the intracellular concentration of this cation, triggering depressive symptoms (33). Vitamin D plays a role in the processes of neuromodulation and neuroplasticity, which appear to be critical in mood regulation. Vitamin D receptor (VDR) gene polymorphism has been demonstrated in people with cognitive impairment and depressive symptoms (39). Epidemiological studies have shown that lower 25(OH)D₃ levels correlate with an increased risk of depression in adults (40). A recent systematic review of the relationship between vitamin D deficiency and antenatal and postnatal depression found that vitamin D (25OHD) levels below 50 nmol/L are associated with a 2.67 higher (OR 3.67; 95% CI 1.72-7.85) risk of depression postpartum compared to persons with a concentration above 50 nmol/L, but no statistically significant relationship was found between low vitamin D levels and depressive symptoms during pregnancy with a 25(OH)D₃ serum limit level of 30 nmol/L.

Oxytocin as a potential biomarker of postpartum depression

The use of biological markers with predictive value for postpartum depression in at-risk women would allow for early treatment, provide support, and minimize the impact on family health and functioning.

In recent years, oxytocin (OT), a hypothalamic peptide hormone known for its role in milk production and secretion during lactation, has been of great interest as a biomarker of postpartum mood disorders (41). Several studies have demonstrated the role that oxytocin plays in the process of adaptation to motherhood (42), as well as in the formation of parent-child bonds.

The importance of oxytocin has also been postulated in the pathogenesis of many mental disorders. In some studies, it has been suggested that depressive symptoms after childbirth have similar hormonal changes as when weaning a child – in both situations the risk of developing mood disorders may, therefore, be elevated (43). Data from animal models suggest the potential role of oxytocin in the development of postpartum depression with the involvement of serotonergic mechanisms (38). An oxytocin anxiolytic effect is postulated (44), however, a small number of studies in humans have shown no therapeutic effect or even mood deterioration after its use (45). In one recent meta-analysis, six out of 2,363 studies on the relationship between oxytocin levels and the occurrence of depression in pregnant or postpartum women were evaluated (46). Four studies confirmed the existence of such a relationship. In the first of these studies, lower oxytocin plasma levels in the third trimester of pregnancy were accompanied by the development of postpartum depressive symptoms (46). The second study found an inverse correlation between serum oxytocin levels in the third trimester of pregnancy and 8 weeks after delivery and the severity of depressive symptoms in lactating women (47). A third study found lower levels of oxytocin in a group of breastfeeding women showing depressive symptoms (48). In the fourth study, however, the presence of a specific subtype of the oxytocin receptor in breastfeeding mothers was associated with lower saliva levels (49). However, other studies have not demonstrated a significant relationship between oxytocin plasma levels and

the presence of depressive symptoms in the mother (50). The inconsistency of results was explained by different methods of oxytocin determination or aggravating factors in medical history as teenage parenthood or preterm birth. Future studies of oxytocin will probably concern fluctuations in serum levels during pregnancy and after delivery to determine the individual profile of changes associated with the susceptibility to depression.

Risk factors for postpartum depression

Taken together, the risk factors for pregnancy and postpartum (maternal) depression include:

- 1) endocrine aspects – changes in hormone levels (significant amplitude of fluctuations in estradiol and stable high glucocorticoid levels);
- 2) deficiency aspects – vitamin D₃, zinc, and magnesium;
- 3) obstetric aspects – specific for postpartum depression: type of delivery and type of delivery anesthesia);
- 4) psychosocial aspects – lack of acceptance of the pregnancy, lack of social support, crisis in a relationship, low socioeconomic status, traumatic life events preceding or during the pregnancy, an informalized relationship (marital status);
- 5) psychopathological aspects – depressive disorders before pregnancy (in these women, 25-50% during pregnancy) (51), seasonal mood swings, alcohol consumption during pregnancy;
- 6) any chronic disease (52).

Anemia has been mentioned in several epidemiological studies as a potential risk factor (52, 53), but others have not confirmed this relationship (54, 55). In one study, the risk of postpartum depression was more than 4 times higher in women with anemia (56), and in a recent meta-analysis (57), the risk in the postpartum period was slightly higher. Stress and anxiety during pregnancy seems to increase the risk of obstetric complications such as premature delivery, preeclampsia, and anemia, as well as the low birth weight of the newborn (58, 59, 60).

Clinical picture of postpartum depression

The clinical picture of depression in the postpartum period resembles that of depression in other periods of life. It has been suggested that a characteristic feature of postpartum depression may be more severe psychomotor drive disorders (agitation and secondary dysphoria) (5). The most commonly reported symptoms in perinatal depression are fatigue and sleep disturbances (55). A relationship has been suggested between the degree of sleep reduction and the severity of depression in postpartum women (56, 57).

The co-occurrence of other psychiatric problems (generalized anxiety disorder, agoraphobia, social phobia, and obsessive-compulsive disorder) with postnatal depression seems to be high but not specific (58, 59).

Specific symptoms of postpartum depression also include changes in the mother-child dyad and often throughout the whole family system. Women with postpartum depression are often more intrusive, less sensitive to changes in the child's emotional state, and showing intermittent and inconsistent patterns of communication with them. The relationship of a child with a depressive mother a few weeks after delivery is characterized by poor mindfulness and communication (visual, voice, and tactile) (60).

Complications of postpartum depression

A mother's depression has a significant impact on both her and her child. The occurrence of depression in pregnancy is accompanied by a deterioration in the course of the pregnancy, and especially by an insufficient weight gain of the child and mother that result from the harmful health behaviors of the mother: poor diet, alcohol consumption, and smoking (61, 62), as well as taking other psychoactive substances (63). Mothers with depression in pregnancy have a higher incidence of hypertension in pregnancy (61) and gestational diabetes (62). Postpartum depression, in turn, causes disorders in the development of mother-child relationships, a decrease in the quality of parental care, and a secondary delay in the child's cognitive, emotional, and motor development (63, 64). It is believed that the delay in the child's development lasts up to adolescence, and children of mothers with postnatal depression show an increased risk of depression, anxiety disorders (including panic disorder), aggressive behavior, and attention deficit hyperactivity disorder at a young age (65, 66).

Depression in the postpartum period is associated with an increased risk of suicide and infanticide (68), and suicide is the leading cause of death for women within 12 months of delivery (69).

Summary

The early diagnosis and proper treatment of gestational and postpartum depression is extremely important for the health of the mother and of the child.

In Poland it is recommended to perform assessments for psychiatric history and adverse life events during routine gestational and perinatal care.

While there is not an established prediction method for postpartum depression, the extant literature supports the existence of a hormone-sensitive postpartum depression phenotype (70). There is sufficient evidence to suggest that reproductive hormone fluctuations trigger affective dysregulation in sensitive women. We should have the appropriate knowledge and skills to assess symptoms of depression and the patient's hormonal status. However no single hormonal test result help in diagnosing of postpartum depression.

Ongoing research will hopefully replicate some of the biomarker findings and lead to novel ways of predicting those at risk to prevent unnecessary suffering for women, their children and families (71). More research is needed in this area.

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