Psychiatr. Pol. 2022; 56(6): 1289–1314
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/10.12740/PP/144138

Biological factors and consequences of pregnancy-related anxiety – What do we know so far?

Agata Mikołajków, Krzysztof Małyszczak

Division of Psychotherapy and Psychosomatic Medicine,
Department and Clinic of Psychiatry, Wroclaw Medical University

Summary

This review aims to sum up the current knowledge about biological factors of pregnancy-related anxiety (PrA) and the most common consequences for both mother and child, thereby identifying the most crucial concerns and suggesting the course of further research in this field. We pursued a literature review using PubMed.

Scientists have shown a significant connection between prenatal anxiety and hormonal changes. These alterations include HPA-axis regulation, thyroid function, oxytocin, prolactin, and progesterone levels. PrA is proven to be a multifactorial condition. Several psychological factors correlate with it, e.g., insufficient social support, unplanned pregnancy, lack of physical activity, and a high level of distress. Although pregnancy is a significant change in one's life and may be a stressful event, it seems inadequate to believe that clinically relevant prenatal anxiety should be explained only by these psychological factors. Pregnancy-related anxiety is a common mental health disorder in pregnancy, and further studies are needed to minimize the risk of its severe consequences.

Key words: pregnancy, pregnancy-related anxiety, anxiety, mental health, biological factors, adverse birth outcomes

Introduction

Psychological and psychiatric conditions in pregnancy have recently been widely discussed. They were suggested to harm both the mother's health and the child's development. While post – and antenatal depression is now receiving growing attention from healthcare providers, the role of prenatal anxiety still seems to be underestimated and underdiagnosed by obstetricians [1].

The reported prevalence of anxiety disorders in pregnancy varies significantly from 9% to 65% [2-22]. This wide range may result from the fact that the concept of pregnancy-related anxiety (PrA) is relatively new and still lacks a proper definition.

It has been suggested to be a distinctive syndrome from generalized anxiety disorder [23-26] and depressive disorder [27]. Huizink et al. [23] created a three-factor model of PrA, which reflected fear of giving birth, fear of bearing a handicapped child, and concern about one's appearance. Symptoms of PrA often include restlessness [28], feeling unfit to cope [29], perception of lack of control, frustration about weight gain, feelings of confusion, dissatisfaction with pregnancy, panic attacks, insomnia, loss of the sense of self, self-doubt, and resentment [25].

As for the course of pregnancy-related anxiety, most researchers claim that it shows a downward trajectory, with symptoms lessening from the first trimester to the third trimester [13, 24, 30–36]. In contrast, others report a stable course [17, 37] or a significant decrease of symptoms in the intermediate stage of gestation [12, 29, 38].

Standard measures used to assess generalized anxiety disorder (GAD) explained only a small part of this condition, so it was crucial to develop new instruments suitable for assessing pregnancy-related anxiety symptoms. Alderdice et al. [39] examined such tools and suggested three of them to be the most appropriate: Prenatal Distress Questionnaire – PDQ [40], Pregnancy-Related Anxiety Scale – PRAS [41], and Pregnancy-Related Anxiety Questionnaire – PRAQ [42]. A shortened 10-item Pregnancy-Related Anxiety Questionnaire-Revised (PRAQ-R) was derived from the original PRAQ containing 34 items [23]. The revised version was designed for use in nulliparous women. To enable this tool's use regardless of parity, a new version was developed: Pregnancy-Related Anxiety Questionnaire-Revised 2 – PRAQ-R2 [43].

This review aims to:

1. Sum up the current knowledge about biological factors contributing to the development of pregnancy-related anxiety:
   a) briefly discuss the contribution of psychological and sociocultural factors on pregnancy-related anxiety,
   b) explain the role of neurotransmitters and immune system in pregnancy-related anxiety,
   c) prepare a comprehensive literature review of hormonal factors leading to pregnancy-related anxiety,
   d) sum up the role of nutritional elements and gut microbiota in the development of prenatal anxiety.
2. Assess the most common consequences of pregnancy-related anxiety for both mother and child.
3. Suggest the course of further research in this field by identifying the most crucial concerns.

Psychological and socio-demographic factors in the development of pregnancy-related anxiety

Multiple psychological and sociocultural factors seem to play an essential role in the development of pregnancy-related anxiety. Women with a lower level of educa-

tion suffer more often from PrA [36]. Most of the papers indicate that younger age is significantly correlated with prenatal anxiety [8, 10], but some claim that older women suffer more often from prenatal anxiety [44]. In contrast, others report no correlation between age and prenatal anxiety whatsoever [45]. Interestingly, researchers show no correlation between marital status or employment status and anxiety symptoms [45], yet household income below $ 20,000 per year is a significant risk factor for PrA [46]. Understandably, multiparous women present with lesser anxiety symptoms in comparison to primiparous women [47].

It seems obvious that being a victim of sexual assault [48] or domestic abuse [49] contributes to anxiety symptoms. Lack of support from a partner also leads to more symptoms of anxiety [50].

Somatic comorbidities play a crucial role in the development of PrA, which include, e.g., hypertensive disorder [5], diabetes [51], obesity [52], and HIV infection [53]. Also, a history of adverse obstetric outcomes significantly increases the chance of suffering from anxiety [54]. Being pregnant by IVF is also linked to a greater frequency of PrA [55].

Both having a history of psychiatric disorders [18] or having any current psychiatric comorbidities during pregnancy [56] significantly increase the risk of prenatal anxiety. A healthy lifestyle acts as a protective factor against anxiety disorders in pregnancy [57].

The premorbid character of a pregnant woman also has a significant impact on the development of PrA. Being optimistic and a feeling of being able to cope [58], high self-esteem [59], resilience [60], extraversion [61] – all act as protective factors against this anxiety disorder. The feeling of low perceived control [59] and neuroticism are well-known risk factors [61].

Biological factors of pregnancy-related anxiety

Neurobiology of Anxiety

The neurobiological mechanisms of anxiety have been widely studied and are well known for various types of anxiety disorders. Stahl [62] gives a comprehensive explanation of how the neurotransmitter response to stimulus determines anxiety symptoms. The amygdala has multiple anatomical connections that allow it to integrate both sensory and cognitive information. Subsequently, it determines whether there should be a fear response or not. The feeling of fear may be regulated by reciprocal connections with the orbitofrontal cortex and anterior cingulate cortex, which regulate emotions. Connections between the amygdala and the periaqueductal gray area of the brainstem determine the motor response to a stimulus (fight, flight, or 'freezing'). Amygdala's connections with the hypothalamus determine the HPA axis response. The connections via the amygdala and locus coeruleus determine the autonomic and cardiovascular response to fear, as the locus coeruleus is abundant with noradrenergic cells. Activation of this area due to a fear-eliciting stimulus triggers a cardiovascular response with increased heart rate and blood pressure. Amygdala function is regulated

by multiple neurotransmitters, such as GABA, serotonin, and noradrenaline. Worrying is linked to cortico-striato-thalamo-cortical (CSTC) feedback loops from the prefrontal cortex. These circuits are regulated by serotonin, GABA, dopamine, noradrenaline, glutamate, and voltage-gated ion channels. The COMT enzyme regulates the availability of dopamine, thereby influencing the presence of anxiety symptoms. Subjects with the Met variant of the enzyme have higher base levels of dopamine than those with the Val variant of COMT. Therefore, stressors can lead to too much dopamine release in these subjects, leading to poor efficiency of information processing under stress. In stressful situations, carriers of the Val variant operate better.

Γ-aminobutyric acid is an inhibitory neurotransmitter. It plays a regulatory role by reducing the activity of many neurons in the amygdala and CSTC loop. Serotonin is the key neurotransmitter that innervates both the amygdala and the CSTC loop elements and regulates fear and worry.

Immune system

The immune and nervous systems work interactively in response to stress. Bartrop et al. [63] discovered that bereaved individuals had decreased lymphocyte function compared to controls. This finding was concordant with results from a prospective longitudinal study by Stein et al. [64], where lymphocyte stimulation responses were researched in spouses of women with breast carcinoma. They found that suppression of mitogen-induced lymphocyte stimulation was a direct consequence of the bereavement event. Moreover, the long-term stress had sensitized subjects to the events of bereavement.

Cytokine profile

Many published research papers support the relationship between cytokine profile and anxiety disorders in pregnancy. Research indicates that the patients suffering from prenatal anxiety present with increased serum pro – and anti-inflammatory cytokines. Moreover, Leff Gelman et al. [65] point out that the dysregulation within the immune system seen in anxiety during pregnancy (increased level of Th1 cytokines and higher ratio of Th1:Th2 cytokines) may contribute to depressive symptoms.

A positive association was observed between anxiety scores and serum levels of: IL-1β [66, 67], IL-2 [65, 68], IL-4 [65], IL-5 [69], IL-6 [65-71], IL-8 [66], IL-9 [68, 69], IL-10 [69], IL-12 [69], IL-13 [69], IL-17A [68], and IL-17B [68]. Many researchers also report a positive link between TNF-α levels and anxiety scores among pregnant women [65-69]. Anxious patients were also observed to present with increased CRP [66].

Endocrine system

Cortisol

Cortisol, also known as the stress hormone, is significantly linked with the development of anxiety disorders. De Brito Guzzo et al. [38] suggest a significant impact of glucocorticoids on the mental state in pregnancy. Anxiety is linked with HPA axis activity as well. Women with higher anxiety levels have significantly elevated cortisol levels [72-74].

Not only the mean level of cortisol seems to have an impact on anxiety. More anxious pregnant women are suggested to have steeper increases in cortisol than less anxious ones [72, 75]. Contrarily, some results implicate a negative association of cortisol levels and anxiety symptoms [75, 76] or no association whatsoever [77]. We hypothesize that these inconsistencies result from a high diurnal variation of cortisol levels, which significantly impedes the interpretation of studies involving cortisol.

SKA2 gene polymorphism may also contribute to anxiety disorders through the increase of the cortisol level [78, 79].

Oxytocin (OT)

Oxytocin is a hormone produced in magno – and parvocellular neurons in the paraventricular nucleus and the hypothalamus's supraoptic nucleus. Subsequently, it is transported by axons to the posterior pituitary and stored until being secreted into the blood [80]. This hormone plays a significant role in pregnancy and postpartum – it is involved in crucial processes, such as uterine muscle contraction during parturition and milk ejection from the mammary gland [81] and has a noticeable impact on neurological function. Oxytocin was shown to modulate stress and social behaviors and to be related to multiple psychiatric disorders in males and females [82]. Anxiogenic and stressful stimuli activate the OT system, which triggers an increase in the activity of OT neurons, OT gene expression, and further peripheral and intracerebral OT release [83]. OT receptors are strongly expressed, among others, in the hippocampus [84], amygdala, and prefrontal cortex [82]. All of these structures were identified to be linked with anxiety and fear expression in humans. The hippocampus is known to modulate HPA-axis sensitivity, thereby regulating the response to stress [85]. It is one of the primary brain areas with a high expression of glucocorticoid receptors. Oxytocin prevents hippocampal neurons from deleterious effects of the stress-induced increase of glucocorticosteroid levels [82]. The central amygdala modulates the GABA-ergic response, playing a crucial role in both active and passive stress responses [86]. The prefrontal cortex also impacts stress appraisal, adaptation, and therefore, stress conditioning [82].

It was proven in the general population that higher OT concentrations are associated with social anxiety disorder. The anxiety disorder probably results from oxytocin receptor malfunction, leading to higher serum OT levels [87]. Moreover, inhibition of oxytocin receptors triggers the release of ACTH and corticosterone [88].

Also, there are reports that prenatal oxytocin exposure is a risk factor both for new-onset anxiety and for the worsening of anxiety symptoms [89]. Pregnant women with higher scores in State-Anxiety Questionnaires presented with higher mean OT levels [51]. Research by Ma et al. [90] supports this thesis – the stressor had a more significant effect in women with higher OT concentrations than in women with low OT concentrations. It is worth mentioning that only OT levels measured without immunoassay extraction are associated with anxiety symptoms [91].

On the contrary, Serati et al. [92] report lower oxytocin levels measured in a blood sample linked with anxiety disorders. Moreover, OT is suggested to have an anxiolytic effect in rats [93] and breastfeeding women [94].

As the data is inconsistent, we suggest that further research in this field is needed to fully understand oxytocin's role in developing an anxiety disorder.

Progesterone

Progesterone was suggested to potentiate GABA activity, which reduces anxiety in pregnant women [38]. Furthermore, finasteride administration, an inhibitor of 5-α-reductase, is followed by increased anxiety [95]. In conclusion, the decrease in progesterone and its metabolites is associated with a higher anxiety level.

Prolactin (PRL)

Prolactin is a polypeptide hormone synthesized in and secreted from lactotrophs, specialized cells of the anterior pituitary gland [96]. It plays an important role not only in lactation and reproduction but also in angiogenesis, immune responses, and osmoregulation [96]. Furthermore, PRL expression was detected in multiple brain regions, such as the hippocampus and amygdala. Also, its secretion is affected by stress [96]. Therefore, PRL was suggested to modulate the neuroendocrine stress axis by the limbic system [97].

Prolactin is believed to have an anxiolytic effect in rats [98] and the general human population [93]. Furthermore, it may be associated with resilience to chronic mild stress [99]. Breastfeeding without formula acts as a protective factor against the development of anxiety symptoms [100, 101]. Brain PRL is supposed to inhibit the HPA axis response during lactation [99]. Also, in the prenatal period, lower PRL levels were associated with more significant anxiety symptoms and increased cortisol levels. Higher levels of PRL resulted in fewer anxiety symptoms and decreased cortisol levels [102].

According to Slattery and Neumann [88], acute or chronic intracerebroventricular (i.c.v.) administration of PRL to female rats resulted in elevated basal plasma levels of ACTH and further attenuated stress-induced secretion of ACTH and corticosterone. PRL seems to counteract the HPA axis actions on the immune system response to stress [88]. Therefore, anxiety disorders may be a consequence of improper secretion of PRL in response to a stressor, as it was reported that in high-trait anxious women,

a stressor did not increase PRL levels in contrast to low-trait anxious women, where PRL levels increased in response to the stressor [103]. On the other hand, female patients with hyperprolactinemia suffer from more significant psychological distress compared to the general population [99]. Further research is needed to better explain this phenomenon.

Thyroid hormones

Thyroid function is widely known to affect mental health. Significant negative correlations were observed between TT4, fT4, fTIs, TT3 levels, and depression scores postpartum [104]. Also, in late pregnancy, TT4 and fT4 concentrations were associated with postpartum depression [105]. Perinatal depression may be predicted by decreased fT4 and thyroxin-binding globulin (TBG) [106], decreased TSH, and elevated anti-TPO antibodies [107].

As for anxiety disorders, the anti-TPO antibody is linked with anxiety in the general population [108]. Moreover, according to Zhou et al [109]., anxiety scores were significantly higher in euthyroid pregnant women with anti-TPO antibodies than in the group of anti-TPO antibody negative patients, probably because anti-TPO antibodies cause a decrease in BDNF and serotonin concentrations in the prefrontal cortex. This mechanism does not need to include changes in the TT4 concentration level [109].

Adiponectin

A positive correlation between serum adiponectin concentrations and anxiety symptoms in the general population was observed [110]. Contrarily, adiponectin was suggested to act anti-inflammatorily by inhibiting such cytokines as TNF-α and IL-6 [111]. Moreover, in line with this research, pregnant women with high-trait anxiety were reported to have a lower adiponectin concentration than those with low-trait anxiety [112].

As these results are inconclusive, it is not yet possible to assume how exactly adiponectin may affect the mental state.

Nutritional elements

Dietary habits are commonly suggested to impact the mental health of pregnant women [113]. Healthy eating patterns reduce the risk of anxiety disorders in pregnancy [114, 115]. Vaz et al. [114] suggested a vegetarian diet to have a positive impact on mental health. Dietary diversity itself is negatively associated with anxiety throughout pregnancy [116]. It was reported that patients with eating disorders present with more severe depression and anxiety [117]. Much research tried to identify the nutritional elements responsible for developing anxiety and depression in pregnant women populations.

Vitamin D is believed to act as a neurosteroid [118], but it is inconsistent with whether it might contribute to anxiety symptoms. While some researchers claim that a lower serum vitamin D level is a significant risk factor for anxiety disorders in pregnancy [119], others report no association [118, 119].

Among amino acids, tryptophan [121, 122], valine, leucine, isoleucine, and phenylalanine [122] may affect pregnant women's mental state. The rates of plasma levels of these amino acids were reported to be inversely correlated with anxiety.

As for microelements, only zinc levels show a non-significant inverse correlation with anxiety [122]. Calcium, magnesium, and copper levels do not influence mental health [120].

Polyunsaturated fatty acids seem to be inversely related to prenatal anxiety. Higher serum DHA, omega-6 (ω-6), and omega-3 (ω-3) PUFA are associated with lower anxiety levels [114, 122, 123]. The mean serum cholesterol level is inversely but not significantly correlated with anxiety symptoms [122].

The plasma choline concentration shows a significant positive association with prenatal anxiety, while betaine levels shows no such association [124].

Gut microbiota

Gut microbiota is believed to be linked with mental health issues [125]. Rackers et al. [126] suggest that it influences mental health through the vagus nerve, gut-secreted neuropeptides, sensory nerves, and cytokines via direct interactions with the intestinal wall, gut permeability, and microbial production of metabolites, such as tryptophan and short-chain fatty acids. The connection between anxiety and gut microbiota changes seems bidirectional since prenatal stress in mice was proven to alter the gut microbiome [126].

The fecal microbial composition alters in women with anxiety disorders in late pregnancy: e.g., *Peptostreptococcaceae* and *Peptococcaceae* are abundant in mothers with higher prenatal anxiety, while *Eubacterium* and *Oscillospira* are observed at higher rates in women with lower prenatal anxiety [127].

Slykerman et al. [128] observed fewer anxiety symptoms in pregnant patients supplemented with the probiotic *Lactobacillus rhamnosus HN001* than in those given placebo. Nonetheless, Dawe et al. [129] reported no positive effect of *Lactobacillus rhamnosus GG* and *Bifidobacterium lactis BB12* on pregnant women's mental health (129).

Vaginal microbiota also seems to be linked with mental health since the risk of bacterial vaginosis is proven to be higher in patients with prenatal anxiety [126]. Finally, it is worth mentioning that fetal gut microbiota is altered in children of highly anxious women as well – a greater abundance of *Proteobacterial* groups and lower relative abundances of lactic acid bacteria and *Bifidobacteria* species have been observed [130].

Outcomes of pregnancy-related anxiety

Anxiety disorders in pregnancy are followed by adverse outcomes both for the mother and her child. Pregnancy-related anxiety was suggested to be a risk factor for hypertensive disorder in pregnancy [131-133] and even preeclampsia [112, 134]. A higher rate of nausea and vomiting was also observed among anxious pregnant patients [112]. Furthermore, researchers noticed correlations between anxiety symptoms in pregnancy and weight gain [47] and a greater chance of postpartum weight retention [135, 136].

As for psychiatric disorders, pregnancy-related anxiety shows high comorbidity with other mental disorders. Researchers noted that PrA might be followed by anxiety disorders later in life [31, 137, 138]. Moreover, prenatal anxiety predicts both antenatal [139] and postpartum depression [29, 50, 112, 140]. Dalke et al. [141] observed that PrA notably increases the risk of suicide and infanticide. Pregnant women with anxiety disorders also suffer from memory deficits [144] and are more likely to use nicotine [47, 143] and illegal substances [144]. Women who present with prenatal anxiety are at higher risk of decreased social and family support [137], report lower sexual satisfaction [145], and more often perceive high parenting stress [146] – it all may lead to a more flawed relationship with the family, partner, and child and subsequently, to higher levels of distress.

Most researchers agree that prenatally anxious women have a lesser probability of breastfeeding [140, 143, 147-149]. Nonetheless, some other studies found no relationship between prenatal anxiety and breastfeeding likelihood [150, 151].

Pregnancy-related anxiety seems to also influence maternal-fetal attachment, both examined prenatally [7, 35, 152-154] and later in the postpartum period [155, 156]. Only one study reports no effect of PrA on maternal-fetal bonding [157].

Significant adverse outcomes were observed not only for the mother but for the child itself. Prenatal anxiety has been proven to be a relevant independent risk factor for preterm birth [16, 27, 132-134, 158, 166]. Elevated cortisol and CRH levels in anxious women are suggested to explain this connection, as these hormones are proposed as a birth-inducing factor [72, 167].

PrA also predicts lower birth weight [16, 133, 134, 158, 165, 166, 168–170] and poorer birth condition, measured as APGAR score [168, 171]. There is a higher risk of delivery complications [172, 173]. Highly anxious women have a greater chance of cesarean section [16, 132, 134, 174–176] and other interventions during labor [174, 177].

What is also very important is that prenatal anxiety was proven to affect HPA-axis regulation on gene expression levels [172-182]. NGF, BDNF, and cortisol levels in the limbic area of children from highly anxious mothers are proven to be improper, altering expected brain development processes and leading to long-lasting changes in emotional behavior [183]. In mice, elevated IL-1β *in utero* was followed by decreased BDNF in the amygdala even in adult offspring [184]. Also, among pregnant women with anxiety, PrA leads to significantly lower BDNF levels in their children than children

of healthy mothers [185]. Increased maternal cortisol may be associated with their children's improper basal cortisol level and irregular cortisol reactivity [170, 186-188]. Furthermore, antenatal anxiety correlates with alterations in EEG results [189] and structural changes [190, 192], involving, e.g., the amygdala[72, 193], prefrontal and premotor cortex [189], temporal lobe [189], and hippocampus [189, 194].

Longitudinally, prenatal anxiety results in infant difficulties [195, 197], such as, e.g., decreased cognitive ability [172, 198, 199] and improper social communication abilities [200-202]. Moreover, children of mothers with anxiety disorders have a higher risk of psychiatric disorders [203], especially those associated with affective problems [72, 101, 196, 203–205]. Some scientists suggest a connection between prenatal anxiety and behavioral difficulties [206, 207], including a greater chance of ADHD diagnosis in children [208, 209]. As a result, maternal anxiety is a risk factor for long-term neuropsychiatric hospitalizations of the child [132].

Antenatal anxiety disorders are also linked with many other conditions diagnosed in children with higher frequency, such as, e.g., bone fractures [210], cardiovascular problems [211, 212], inflammatory diseases [213, 215], respiratory tract infections, and infant colic [213, 216].

Conclusions

The issue of pregnancy-related anxiety is extremely important since it is significantly positively associated with adverse birth outcomes; due to prenatal anxiety, the risk of preterm birth, low birth weight, and delivery complications increases. Moreover, children of prenatally anxious mothers presented many long-lasting developmental problems and a greater chance of neuropsychiatric disorder diagnosis.

Although it has been proven that lifetime costs per mother with perinatal anxiety are incredibly high [217], it is still an underrated and underdiagnosed issue. Smith et al. [218] point out that knowledge regarding this condition is still meager, with only 4.7 % of respondents listing anxiety and other mental disorders as the most frequent pregnancy-related issues. Moreover, it has been shown that GPs often do not recognize it [219]. Pregnant women with anxiety, not being aware of such conditions as PrA, seek information around depression. As this information is often not relevant, they get confused and are left with a feeling of alienation and lack of understanding [25].

Pregnancy-related anxiety is proven to be a multifactorial condition. Several psychological factors are listed to correlate with it, such as, e.g., insufficient social support [4, 18, 49, 220], unplanned pregnancy [2, 11, 21, 221], lack of physical activity [36, 57, 222, 223] and high level of distress [17, 18, 56, 58]. Although pregnancy is obviously a significant change to one's life and, therefore, may be a reason for distress, it seems inadequate to believe that clinically relevant prenatal anxiety should be explained only by these psychological factors.

Many biological factors are now suggested to be associated with anxiety symptoms in pregnancy. Scientists have shown a significant connection between prenatal

anxiety and hormonal changes. These alterations include not only HPA-axis regulation or thyroid function but also, e.g., oxytocin, prolactin, or progesterone levels. Nutritional elements and gut microbiota are also believed to influence the mental state of pregnancy. Even though research on biological factors leading to prenatal anxiety has been begun, the pathogenesis of PrA is still unclear. Although the number of studies is increasing, it is still scarce, and results are often inconclusive. Therefore, we believe that psychiatrists should focus on this problem to better understand the risk factors of prenatal anxiety. With a greater understanding of this condition, it would be possible to diagnose and treat anxious pregnant women more successfully, resulting in fewer severe consequences that prenatal anxiety is proven to be associated with.

Although the mechanisms of neurotransmitter actions and the HPA axis seem to be understood reasonably well, there is a lack of conclusive literature regarding the link between hormonal changes and prenatal anxiety. We believe that further research should focus on the role of endocrine system alterations in the development of PrA. Furthermore, due to the great frequency of PrA within the pregnant population, we would like to underline the importance of using screening tools for prenatal anxiety by physicians. We have read only one Polish publication regarding prenatal anxiety [8], which may indicate the lack of interest of Polish healthcare professionals in this area. Also, there are no clear Polish guidelines for the management of PrA. Unfortunately, despite such screening tools in English (e.g., Pregnancy-Related Anxiety Questionnaire-Revised 2[43]), we lack Polish adaptions. Therefore, we believe that Polish researchers should aim to create such tools.

References

1. Thorsness KR, Watson C, LaRusso EM. *Perinatal anxiety: Approach to diagnosis and management in the obstetric setting.* Am. J. Obstet. Gynecol. 2018; 219(4): 326–345. Available from: https://doi.org/10.1016/j.ajog.2018.05.017
2. Alqahtani AH, Al Khedair K, Al-Jeheiman R, Al-Turki HA, Al Qahtani NH. *Anxiety and depression during pregnancy in women attending clinics in a University Hospital in Eastern province of Saudi Arabia: Prevalence and associated factors.* Int. J. Womens Health 2018; 10: 101–108.
3. Fairbrother N, Janssen P, Antony MM, Tucker E, Young AH. *Perinatal anxiety disorder prevalence and incidence.* J. Affect. Disord. 2016; 200: 148–155. Available from: http://dx.doi.org/10.1016/j.jad.2015.12.082
4. Ghaffar R, Iqbal Q, Khalid A, Saleem F, Hassali MA, Baloch NS et al. *Frequency and predictors of anxiety and depression among pregnant women attending tertiary healthcare institutes of Quetta City, Pakistan.* BMC Womens Health 2017; 17(1): 51.
5. Kang YT, Yao Y, Dou J, Guo X, Li SY, Zhao CN et al. *Prevalence and risk factors of maternal anxiety in late pregnancy in China.* Int. J. Environ. Res. Public Health 2016; 13(5): 468.
6. Nath A, Venkatesh S, Balan S, Metgud CS, Krishna M, Murthy GVS. *The prevalence and determinants of pregnancy-related anxiety amongst pregnant women at less than 24 weeks of pregnancy in Bangalore, Southern India.* Int. J. Womens Health 2019; 11: 241–248.

7. Nagle-Yang S, Phillips M, Albaugh A, Zhao L, Amin J, Ahmad E et al. *Depression, anxiety, and attachment among women hospitalized on an antepartum unit.* Int. J. Psychiatry Med. 2019; 54(6): 395–407.
8. Makara-Studzińska M, Morylowska-Topolska J, Sygit K, Sygit M, Goździewska M. *Socio-demographical and psychosocial determinants of anxiety symptoms in a population of pregnant women in the regions of central and eastern Poland.* Ann. Agric. Environ. Med. 2013; 20(1): 195–202.
9. Redinger S, Norris SA, Pearson RM, Richter L, Rochat T. *First trimester antenatal depression and anxiety: Prevalence and associated factors in an urban population in Soweto, South Africa.* J. Dev. Orig. Health Dis. 2018; 9(1): 30–40.
10. Rubertsson C, Hellström J, Cross M, Sydsjö G. *Anxiety in early pregnancy: Prevalence and contributing factors.* Arch. Womens Ment. Health 2014; 17(3): 221–228.
11. Silva MM de J, Nogueira DA, Clapis MJ, Leite EPRC. *Anxiety in pregnancy: Prevalence and associated factors.* Rev. da Esc. Enferm. 2017; 51: e03253.
12. Soto-Balbuena C, Rodríguez M de la F, Gomis AIE, Barriendos FJF, Le HN, Blanco CF et al. *Incidence, prevalence and risk factors related to anxiety symptoms during pregnancy.* Psicothema 2018; 30(3): 257–263.
13. Zhang Y, Muyiduli X, Wang S, Jiang W, Wu J, Li M et al. *Prevalence and relevant factors of anxiety and depression among pregnant women in a cohort study from south-east China.* J. Reprod. Infant. Psychol. 2018; 36(5): 519–529. Available from: https://doi.org/10.1080/02646838.2018.1492098
14. Uguz F, Yakut E, Aydogan S, Bayman MG, Gezginc K. *Prevalence of mood and anxiety disorders during pregnancy: A case-control study with a large sample size.* Psychiatry Res. 2019; 272: 316–318. Available from: https://doi.org/10.1016/j.psychres.2018.12.129
15. Zhu CS, Tan TC, Chen HY, Malhotra R, Allen JC, Østbye T. *Threatened miscarriage and depressive and anxiety symptoms among women and partners in early pregnancy.* J. Affect. Disord. 2018; 237: 1–9. Available from: https://doi.org/10.1016/j.jad.2018.04.012
16. Wallwiener S, Goetz M, Lanfer A, Gillessen A, Suling M, Feisst M et al. *Epidemiology of mental disorders during pregnancy and link to birth outcome: A large-scale retrospective observational database study including 38,000 pregnancies.* Arch. Gynecol. Obstet. 2019; 299(3): 755–763. Available from: https://doi.org/10.1007/s00404-019-05075-2
17. Ahmed A, Feng C, Bowen A, Muhajarine N. *Latent trajectory groups of perinatal depressive and anxiety symptoms from pregnancy to early post-partum and their antenatal risk factors.* Arch. Womens Ment. Health 2018; 21(6): 689–698.
18. Bayrampour H, McDonald S, Tough S. *Risk factors of transient and persistent anxiety during pregnancy.* Midwifery 2015; 31(6): 582–589. Available from: http://dx.doi.org/10.1016/j.midw.2015.02.009
19. Dikmen-Yildiz P, Ayers S, Phillips L. *Depression, anxiety, PTSD and comorbidity in perinatal women in Turkey: A longitudinal population-based study.* Midwifery 2017; 55 :29–37. Available from: http://dx.doi.org/10.1016/j.midw.2017.09.001
20. Bhushan NL, Krupp K, Jaykrishna P, Ravi K, Khan A, Shidhaye R et al. *The association between social support through contacts with Accredited Social Health Activists (ASHAs) and antenatal anxiety among women in Mysore, India: A cross-sectional study.* Soc. Psychiatry Psychiatr. Epidemiol. 2020; 55(10): 1323-1333. Available from: https://doi.org/10.1007/s00127-020-01854-4
21. Fadzil A, Balakrishnan K, Razali R, Sidi H, Malapan T, Japaraj RP et al. *Risk factors for depression and anxiety among pregnant women in Hospital Tuanku Bainun, Ipoh, Malaysia.* Asia Pac. Psychiatry 2013; 5(Suppl 1): 7–13.

22. Ferreira CR, Orsini MC, Vieira CR, do Amarante Paffaro AM, Silva RR. *Prevalence of anxiety symptoms and depression in the third gestational trimester.* Arch. Gynecol. Obstet. 2015; 291(5): 999–1003.
23. Huizink AC, Mulder EJH, Robles De Medina PG, Visser GHA, Buitelaar JK. *Is pregnancy anxiety a distinctive syndrome?* Early Hum. Dev. 2004; 79(2): 81–91.
24. Brunton R, Dryer R, Saliba A, Kohlhoff J. *Re-examining pregnancy-related anxiety: A replication study.* Women and Birth 2019; 32(1): e131–137.
25. Highet N, Stevenson AL, Purtell C, Coo S. *Qualitative insights into women's personal experiences of perinatal depression and anxiety.* Women and Birth 2014; 27(3): 179–184.
26. Blackmore ER, Gustafsson H, Gilchrist M, Wyman C, O'Connor TG. *Pregnancy-related anxiety: Evidence of distinct clinical significance from a prospective longitudinal study.* J. Affect. Disord. 2016; 197: 251–258.
27. Orr ST, Reiter JP, Blazer DG, James SA. *Maternal prenatal pregnancy-related anxiety and spontaneous preterm birth in Baltimore, Maryland.* Psychosom. Med. 2007; 69(6): 566–570.
28. Petrovic D, Perovic M, Lazovic B, Pantic I. *Association between walking, dysphoric mood and anxiety in late pregnancy: A cross-sectional study.* Psychiatry Res. 2016; 246(July): 360–363. Available from: http://dx.doi.org/10.1016/j.psychres.2016.10.009
29. Rallis S, Skouteris H, McCabe M, Milgrom J. *A prospective examination of depression, anxiety and stress throughout pregnancy.* Women Birth. 2014; 27(4): e36–42. Available from: http://dx.doi.org/10.1016/j.wombi.2014.08.002
30. Canário C, Figueiredo B. *Anxiety and depressive symptoms in women and men from early pregnancy to 30 months post-partum.* J. Reprod. Infant. Psychol. 2017; 35(5): 431–449. Available from: http://doi.org/10.1080/02646838.2017.1368464
31. Huizink AC, Menting B, Oosterman M, Verhage ML, Kunseler FC, Schuengel C. *The interrelationship between pregnancy-specific anxiety and general anxiety across pregnancy: A longitudinal study.* J. Psychosom. Obstet. Gynecol. 2014; 35(3): 92–100.
32. Huang MZ, Kao CH, Lin KC, Hwang JL, Puthussery S, Gau ML. *Psychological health of women who have conceived using assisted reproductive technology in Taiwan: Findings from a longitudinal study.* BMC Womens Health 2019; 19(1): 97.
33. Lou S, Mikkelsen L, Hvidman L, Petersen OB, Nielsen CP. *Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review.* Acta Obstet. Gynecol. Scand. 2015; 94(1): 15–27.
34. Madigan S, Wade M, Plamondon A, Vaillancourt K, Jenkins JM, Shouldice M et al. *Course of depression and anxiety symptoms during the transition to parenthood for female adolescents with histories of victimization.* Child Abus. Negl. 2014; 38(7): 1160–1170. Available from: http://dx.doi.org/10.1016/j.chiabu.2014.04.002
35. Udry-Jørgensen L, Darwiche J, Germond M, Wunder D, Vial Y. *Anxiety, depression, and attachment before and after the first-trimester screening for Down syndrome: Comparing couples who undergo ART with those who conceive spontaneously.* Prenat. Diagn. 2015; 35(13): 1287–1293.
36. Loo van de KFE, Vlenterie R, Nikkels SJ, Merkus PJFM, Roukema J, Verhaak CM et al. *Depression and anxiety during pregnancy: The influence of maternal characteristics.* Birth 2018; 45(4): 478–489.
37. Mudra S, Göbel A, Barkmann C, Goletzke J, Hecher K, Schulte-Markwort M et al. *The longitudinal course of pregnancy-related anxiety in parous and nulliparous women and its association with symptoms of social and generalized anxiety.* J. Affect. Disord. 2020; 260: 111–118. Available from: https://doi.org/10.1016/j.jad.2019.08.033

38. Brito Guzzo de SFC, Rafael C, Matheus Fitipaldi B, Amarylis Garcia A, Vinícius Dias K, Luiz YJ et al. *Impact of chronic stressors on the anxiety profile of pregnant rats.* Physiol. Behav. 2015; 142: 137–145. Available from: http://dx.doi.org/10.1016/j.physbeh.2015.02.014

39. Alderdice F, Lynn F, Lobel M. *A review and psychometric evaluation of pregnancy-specific stress measures.* J. Psychosom. Obstet. Gynecol. 2012; 33(2): 62–77.

40. Yali AM, Lobel M. *Coping and distress in pregnancy: An investigation of medically high risk women.* J. Psychosom. Obstet. Gynaecol. 1999; 20(1): 39–52.

41. Wadhwa PD, Sandman CA, Porto M, Dunkel-Schetter C, Garite TJ. *The association between prenatal stress and infant birth weight and gestational age at birth: A prospective investigation.* Am. J. Obstet. Gynecol. 1993; 169(4): 858–865. Available from: http://dx.doi.org/10.1016/0002-9378(93)90016-C

42. Van den Bergh BR. *The influence of maternal emotions during pregnancy on fetal and neonatal behavior.* J. Prenat. Perinat. Psychol. Health 1990; 5(2): 119–128.

43. Huizink AC, Delforterie MJ, Scheinin NM, Tolvanen M, Karlsson L, Karlsson H. *Adaption of pregnancy anxiety questionnaire–revised for all pregnant women regardless of parity: PRAQ-R2.* Arch. Womens Ment. Health 2016; 19(1): 125–132. Available from: http://dx.doi.org/10.1007/s00737-015-0531-2

44. Ma X, Wang Y, Hu H, Tao XG, Zhang Y, Shi H. *The impact of resilience on prenatal anxiety and depression among pregnant women in Shanghai.* J. Affect. Disord. 2019; 250(August 2018): 57–64.

45. Furtado M, Chow CHT, Owais S, Frey BN, Van Lieshout RJ. *Risk factors of new onset anxiety and anxiety exacerbation in the perinatal period: A systematic review and meta-analysis.* J. Affect. Disord. 2018; 238: 626–635. Available from: https://doi.org/10.1016/j.jad.2018.05.073

46. Hui AL, Sevenhuysen G, Harvey D, Salamon E. *Stress and anxiety in women with gestational diabetes during dietary management.* Diabetes Educ. 2014; 40(5): 668–677.

47. Westerneng M, Witteveen AB, Warmelink JC, Spelten E, Honig A, de Cock P. *Pregnancy-specific anxiety and its association with background characteristics and health-related behaviors in a low-risk population.* Compr. Psychiatry 2017; 75: 6–13. Available from: http://dx.doi.org/10.1016/j.comppsych.2017.02.002

48. Tinglöf S, Högberg U, Lundell IW, Svanberg AS. *Exposure to violence among women with unwanted pregnancies and the association with post-traumatic stress disorder, symptoms of anxiety and depression.* Sex. Reprod. Health 2015; 6(2): 50–53. Available from: http://dx.doi.org/10.1016/j.srhc.2014.08.003

49. Bayrampour H, Vinturache A, Hetherington E, Lorenzetti DL, Tough S. *Risk factors for antenatal anxiety: A systematic review of the literature.* J. Reprod. Infant. Psychol. 2018; 36(5): 476–503. Available from: https://doi.org/10.1080/02646838.2018.1492097

50. Biaggi A, Conroy S, Pawlby S, Pariante CM. *Identifying the women at risk of antenatal anxiety and depression: A systematic review.* J. Affect. Disord. 2016; 191: 62–77. Available from: http://dx.doi.org/10.1016/j.jad.2015.11.014

51. Lara-Cinisomo S, D'Anna-Hernandez K, Fujimoto EM, Pedersen CA. *Exploring associations between perinatal depression, anxiety, and urinary oxytocin levels in Latinas.* Arch. Womens Ment. Health 2019; 22(4): 447–455.

52. Holton S, Fisher J, Nguyen H, Brown WJ, Tran T. *Pre-pregnancy body mass index and the risk of antenatal depression and anxiety.* Women and Birth 2019; 32(6): e508–514. Available from: https://doi.org/10.1016/j.wombi.2019.01.007

53. Aaron E, Bonacquisti A, Geller PA, Polansky M. *Perinatal depression and anxiety in women with and without human immunodeficiency virus infection.* Womens Health Issues 2015; 25(5): 579–585. Available from: http://dx.doi.org/10.1016/j.whi.2015.04.003

54. Gravensteen IK, Jacobsen EM, Sandset PM, Helgadottir LB, Rådestad I, Sandvik L et al. *Anxiety, depression and relationship satisfaction in the pregnancy following stillbirth and after the birth of a live-born baby: A prospective study.* BMC Pregnancy Childbirth 2018; 18(1): 41.

55. García-Blanco A, Diago V, Hervás D, Ghosn F, Vento M, Cháfer-Pericás C. *Anxiety and depressive symptoms, and stress biomarkers in pregnant women after in vitro fertilization: A prospective cohort study.* Hum. Reprod. 2018; 33(7): 1237–1246.

56. Barthel D, Kriston L, Barkmann C, Appiah-Poku J, Te Bonle M, Esther Doris KY et al. *Longitudinal course of ante – and postpartum generalized anxiety symptoms and associated factors in West-African women from Ghana and ZAF.* J. Affect. Disord. 2016; 197: 125–133. Available from: http://dx.doi.org/10.1016/j.jad.2016.03.014

57. Padmapriya N, Bernard JY, Liang S, Loy SL, Shen Z, Kwek K et al. *Association of physical activity and sedentary behavior with depression and anxiety symptoms during pregnancy in a multiethnic cohort of Asian women.* Arch. Womens Ment. Health 2016; 19(6): 1119–1128. Available from: http://dx.doi.org/10.1007/s00737-016-0664-y

58. Barber CC, Starkey NJ. *Predictors of anxiety among pregnant New Zealand women hospitalised for complications and a community comparison group.* Midwifery 2015; 31(9): 888–896. Available from: http://dx.doi.org/10.1016/j.midw.2015.04.017

59. Dunkel Schetter C, Niles AN, Guardino CM, Khaled M, Kramer MS. *Demographic, medical, and psychosocial predictors of pregnancy anxiety.* Paediatr. Perinat. Epidemiol. 2016; 30(5): 421–429.

60. Roos A, Faure S, Lochner C, Vythilingum B, Stein DJ. *Predictors of distress and anxiety during pregnancy.* Afr. J. Psychiatry (Johannesbg) 2013; 16(2): 118–122.

61. Meijer JL, Bockting CLH, Stolk RP, Kotov R, Ormel J, Burger H. *Associations of life events during pregnancy with longitudinal change in symptoms of antenatal anxiety and depression.* Midwifery 2014; 30(5): 526–531. Available from: http://dx.doi.org/10.1016/j.midw.2013.06.008

62. Stahl SM, editor. *Stahl's essential psychopharmacology. Neuroscientific basis and practical applications*, 4th ed. Cambridge: Cambridge Medicine; 2020. pp. 392–397.

63. Bartrop RW, Lazarus L, Luckhurst E, Kiloh LG, Penny R. *Depressed lymphocyte function after bereavement.* Lancet 1977; 309(8016): 834–836.

64. Stein M, Keller SE, Schleifer SJ. *Immune system. Relationship to anxiety disorders.* Psychiatr. Clin. North Am. 1988; 11(2): 349–360. Available from: https://doi.org/10.1016/S0193-953X(18)30502-1

65. Leff Gelman P, Mancilla-Herrera I, Flores-Ramos M, Saravia Takashima MF, Cruz Coronel FM, Cruz Fuentes C et al. *The cytokine profile of women with severe anxiety and depression during pregnancy.* BMC Psychiatry 2019; 19(1): 104.

66. Vieira MMM, Ferreira TB, Pacheco PAF, Barros PO, Almeida CRM, Araújo-Lima CF et al. *Enhanced Th17 phenotype in individuals with generalized anxiety disorder.* J. Neuroimmunol. 2010; 229(1–2): 212–218. Available from: http://dx.doi.org/10.1016/j.jneuroim.2010.07.018

67. Solati J, Kleehaupt E, Kratz O, Moll GH, Golub Y. *Inverse effects of lipopolysaccharides on anxiety in pregnant mice and their offspring.* Physiol. Behav. 2015; 139: 369–374. Available from: http://dx.doi.org/10.1016/j.physbeh.2014.10.016

68. Coussons-Read ME, Okun ML, Schmitt MP, Giese S. *Prenatal stress alters cytokine levels in a manner that may endanger human pregnancy.* Psychosom. Med. 2005; 67(4): 625–631.

69. Karlsson L, Nousiainen N, Scheinin NM, Maksimow M, Salmi M, Lehto SM et al. *Cytokine profile and maternal depression and anxiety symptoms in mid-pregnancy—the FinnBrain Birth Cohort Study.* Arch. Womens Ment. Health 2017; 20(1): 39–48. Available from: http://dx.doi.org/10.1007/s00737-016-0672-y

70. Fishe KJ, Tell D, Mathews HL, Witek Janusek L. *136. Pregnancy specific anxiety and distress is related to increased IL-6 during the second trimester of pregnancy.* Brain Behav. Immun. 2013; 32(Suppl): e39–40. Available from: http://dx.doi.org/10.1016/j.bbi.2013.07.148

71. Osborne LM, Brar A, Klein SL. *The role of Th17 cells in the pathophysiology of pregnancy and perinatal mood and anxiety disorders.* Brain Behav. Immun. 2019; 76: 7–16. Available from: https://doi.org/10.1016/j.bbi.2018.11.015

72. Kane HS, Dunkel Schetter C, Glynn LM, Hobel CJ, Sandman CA. *Pregnancy anxiety and prenatal cortisol trajectories.* Biol. Psychol. 2014; 100(1): 13–9. Available from: http://dx.doi.org/10.1016/j.biopsycho.2014.04.003

73. Paskulin JTA, Drehmer M, Olinto MT, Hoffmann JF, Pinheiro AP, Schmidt MI et al. *Association between dietary patterns and mental disorders in pregnant women in southern Brazil.* Rev. Bras. Psiquiatr. 2017; 39(3): 208–215.

74. Valsamakis G, Papatheodorou DC, Chalarakis N, Vrachnis NN, Sidiropoulou EJ, Manolikaki M et al. *In pregnancy increased maternal STAI trait stress score shows decreased insulin sensitivity and increased stress hormones.* Psychoneuroendocrinology 2017; 84: 11–16. Available from: http://dx.doi.org/10.1016/j.psyneuen.2017.06.008

75. Orta OR, Tworoger SS, Terry KL, Coull BA, Gelaye B, Kirschbaum C et al. *Stress and hair cortisol concentrations from preconception to the third trimester.* Stress 2019; 22(1): 60–69. Available from: https://doi.org/10.1080/10253890.2018.1504917

76. Stalder T, Steudte-Schmiedgen S, Alexander N, Klucken T, Vater A, Wichmann S et al. *Stress-related and basic determinants of hair cortisol in humans: A meta-analysis*. Psychoneuroendocrinology 2017; 77: 261–274. Available from: http://dx.doi.org/10.1016/j.psyneuen.2016.12.017

77. Mustonen P, Karlsson L, Scheinin NM, Kortesluoma S, Coimbra B, Rodrigues AJ et al. *Hair cortisol concentration (HCC) as a measure for prenatal psychological distress — A systematic review.* Psychoneuroendocrinology 2018; 92: 21–8. Available from: https://doi.org/10.1016/j.psyneuen.2018.03.019

78. Guintivano J, Brown T, Newcomer A, Jones M, Cox O, Maher BS et al. *Identification and replication of a combined epigenetic and genetic biomarker predicting suicide and suicidal behaviors.* Am. J. Psychiatry 2014; 171(12): 1287–1296.

79. Ijabi J, Moradi-Sardareh H, Afrisham R, Seifi F, Ijabi R. *SKA2 gene – A novel biomarker for latent anxiety and preterm birth prediction.* Eur. J. Obstet. Gynecol. Reprod. Biol. 2019; 237: 106–112.

80. Gimpl G, Fahrenholz F. *The oxytocin receptor system: Structure, function, and regulation.* Physiol. Rev. 2001; 81(2): 629–683.

81. Gruber CW. *Physiology of invertebrate oxytocin and vasopressin neuropeptides.* Exp. Physiol. 2014; 99(1): 55–61.

82. Matsushita H, Latt HM, Koga Y, Nishiki T, Matsui H. *Oxytocin and stress: Neural mechanisms, stress-related disorders, and therapeutic approaches.* Neuroscience 2019; 417: 1–10. Available from: https://doi.org/10.1016/j.neuroscience.2019.07.046

83. Neumann ID, Slattery DA. *Oxytocin in general anxiety and social fear: A translational approach.* Biol. Psychiatry 2016; 79(3): 213–221. Available from: http://dx.doi.org/10.1016/j.biopsych.2015.06.004

84. Tomizawa K, Iga N, Lu YF, Moriwaki A, Matsushita M, Li ST et al. *Oxytocin improves long-lasting spatial memory during motherhood through MAP kinase cascade.* Nat. Neurosci. 2003; 6(4): 384–390.

85. Windle RJ, Shanks N, Lightman SL, Ingram CD. *Central oxytocin administration reduces stress-induced corticosterone release and anxiety behavior in rats.* Endocrinology 1997; 138(7): 2829–2834.

86. Gozzi A, Jain A, Giovanelli A, Bertollini C, Crestan V, Schwarz AJ et al. *A neural switch for active and passive fear.* Neuron 2010; 67(4): 656–666. Available from: http://dx.doi.org/10.1016/j.neuron.2010.07.008

87. Hoge EA, Pollack MH, Kaufman RE, Zak PJ, Simon NM. *Oxytocin levels in social anxiety disorder.* CNS Neurosci. Ther. 2008; 14(3): 165–170.

88. Slattery DA, Neumann ID. *No stress please! Mechanisms of stress hyporesponsiveness of the maternal brain.* J. Physiol. 2008; 586(2): 377–385.

89. Kroll-Desrosiers AR, Nephew BC, Babb JA, Guilarte-Walker Y, Moore Simas TA, Deligiannidis KM. *Association of peripartum synthetic oxytocin administration and depressive and anxiety disorders within the first postpartum year.* Depress. Anxiety 2017; 34(2): 137–146.

90. Ma X, Wei Q, Jiang Z, Shi Y, Zhang Y, Shi H. *The role of serum oxytocin levels in the second trimester in regulating prenatal anxiety and depression: A sample from Shanghai Maternal-Child Pairs Cohort study.* J. Affect. Disord. 2020; 264: 150–156. Available from: https://doi.org/10.1016/j.jad.2019.12.019

91. Saxbe D, Khaled M, Horton KT, Mendez AJ. *Maternal prenatal plasma oxytocin is positively associated with prenatal psychological symptoms, but method of immunoassay extraction may affect results.* Biol. Psychol. 2019; 147: 107718. Available from: https://doi.org/10.1016/j.biopsycho.2019.107718

92. Serati M, Grassi S, Redaelli M, Pergoli L, Cantone L, La Vecchia A et al. *Is there an association between oxytocin levels in plasma and pregnant women's mental health?* J. Am. Psychiatr. Nurses Assoc. 2021; 27(3): 222–230.

93. Neumann ID. *Brain mechanisms underlying emotional alterations in the peripartum period in rats.* Depress. Anxiety 2003; 17(3): 111–121.

94. Stuebe AM, Grewen K, Meltzer-Brody S. *Association between maternal mood and oxytocin response to breastfeeding.* J. Womens Health (Larchmt.) 2013; 22(4): 352–361.

95. Faturi C de B, Teixeira-Silva F, Leite JR. *The anxiolytic effect of pregnancy in rats is reversed by finasteride.* Pharmacol. Biochem. Behav. 2006; 85(3): 569–574.

96. Gregerson KA. *Prolactin: Structure, function, and regulation of secretion.* In: Neill JD, editor. *Knobil Neill's physiology of reproduction.* Amsterdam: Elsevier; 2006. pp. 1703–1726.

97. Salais-López H, Lanuza E, Agustín-Pavón C, Martínez-García F. *Tuning the brain for motherhood: Prolactin-like central signalling in virgin, pregnant, and lactating female mice.* Brain Struct. Funct. 2017; 222(2): 895–921.

98. Torner L, Toschi N, Pohlinger A, Landgraf R, Neumann ID. *Anxiolytic and anti-stress effects of brain prolactin: Improved efficacy of antisense targeting of the prolactin receptor by molecular modeling.* J. Neurosci. 2001; 21(9): 3207–3214.

99. Torner L. *Actions of prolactin in the brain: From physiological adaptations to stress and neurogenesis to psychopathology.* Front. Endocrinol. (Lausanne) 2016; 7: 25.

100. Srkalović Imširagić A, Begić D, Šimičević L, Bajić Ž. *Prediction of posttraumatic stress disorder symptomatology after childbirth – A Croatian longitudinal study.* Women Birth 2017; 30(1): e17–e23.

101. Agrati D, Browne D, Jonas W, Meaney M, Atkinson L, Steiner M et al. *Maternal anxiety from pregnancy to 2 years postpartum: Transactional patterns of maternal early adversity and child temperament.* Arch. Womens Ment. Health 2015; 18(5): 693–705.

102. Zhang H, Shao S, Su Q, Yao D, Sun H, Ding D et al. *Involvement of prolactin in newborn infant irritability following maternal perinatal anxiety symptoms.* J. Affect. Disord. 2018; 238: 526–533.

103. Demyttenaere K, Nijs P, Evers-Kiebooms G, Koninckx PR. *The effect of a specific emotional stressor on prolactin, cortisol, and testosterone concentrations in women varies with their trait anxiety.* Fertil. Steril. 1989; 52(6): 942–948. Available from: http://dx.doi.org/10.1016/S0015-0282(16)53156-2

104. Pedersen CA. *Postpartum mood and anxiety disorders: A guide for the nonpsychiatric clinician with an aside on thyroid associations with postpartum mood.* Thyroid 1999; 9(7): 691–697.

105. Pedersen CA, Johnson JL, Silva S, Bunevicius R, Meltzer-Brody S, Hamer RM et al. *Antenatal thyroid correlates of postpartum depression.* Psychoneuroendocrinology 2007; 32(3): 235–245.

106. Pedersen C, Leserman J, Garcia N, Stansbury M, Meltzer-Brody S, Johnson J. *Late pregnancy thyroid-binding globulin predicts perinatal depression.* Psychoneuroendocrinology 2016; 65: 84–93. Available from: http://dx.doi.org/10.1016/j.psyneuen.2015.12.010

107. Pop VJ, Wijnen HA, Lapkienne L, Bunivicius R, Vader HL, Essed GG. *The relation between gestational thyroid parameters and depression: A reflection of the downregulation of the immune system during pregnancy?* Thyroid 2006; 16(5): 485–492.

108. Carta MG, Loviselli A, Hardoy MC, Massa S, Cadeddu M, Sardu C et al. *The link between thyroid autoimmunity (antithyroid peroxidase autoantibodies) with anxiety and mood disorders in the community: A field of interest for public health in the future.* BMC Psychiatry 2004; 4: 25.

109. Zhou Y, Wang X, Zhao Y, Liu A, Zhao T, Zhang Y et al. *Elevated thyroid peroxidase antibody increases risk of post-partum depression by decreasing prefrontal cortex BDNF and 5-HT levels in mice.* Front. Cell Neurosci. 2017; 10: 307.

110. Wilhelm CJ, Choi D, Huckans M, Manthe L, Loftis JM. *Adipocytokine signaling is altered in flinders sensitive line rats, and adiponectin correlates in humans with some symptoms of depression.* Pharmacol. Biochem. Behav. 2013; 103(3): 643–651. Available from: http://dx.doi.org/10.1016/j.pbb.2012.11.001

111. Gill J, Vythilingam M, Page GG. *Low cortisol, high DHEA, and high levels of stimulated TNF-α, and IL-6 in women with PTSD.* J. of Traumatic Stress 2008; 21(6): 530–539.

112. Rebelo F, Jesus Pereira Pinto de T, Franco-Sena AB, Lepsch J, Benaim C, Struchiner CJ et al. *Plasma adiponectin is inversely associated with antenatal anxiety: Results from a Brazilian cohort.* Psychoneuroendocrinology 2015; 51: 92–100. Available from: http://dx.doi.org/10.1016/j.psyneuen.2014.09.015

113. Siegel RS, Brandon AR. *Adolescents, pregnancy, and mental health.* J. Pediatr. Adolesc. Gynecol. 2014; 27(3): 138–150. Available from: http://dx.doi.org/10.1016/j.jpag.2013.09.008

114. Vaz Jdos S, Kac G, Emmett P, Davis JM, Golding J, Hibbeln JR. *Dietary patterns, n-3 fatty acids intake from seafood and high levels of anxiety symptoms during pregnancy: Findings from the Avon Longitudinal Study of Parents and Children.* PLoS One 2013; 8(7): e67671.

115. Vilela AAF, Pinto T de JP, Rebelo F, Benaim C, Lepsch J, Dias-Silva CH et al. *Association of prepregnancy dietary patterns and anxiety symptoms from midpregnancy to early postpartum in a prospective cohort of Brazilian women.* J. Acad. Nutr. Diet. 2015; 115(10): 1626–1635. Available from: http://dx.doi.org/10.1016/j.jand.2015.01.007

116. Jiang W, Mo M, Li M, Wang S, Muyiduli X, Shao B et al. *The relationship of dietary diversity score with depression and anxiety among prenatal and post-partum women.* J. Obstet. Gynaecol. Res. 2018; 44(10): 1929–1936.

117. Dos Santos AM, Benute GRG, Dos Santos NO, Nomura RMY, Lucia de MCS, Francisco RPV. *Presence of eating disorders and its relationship to anxiety and depression in pregnant women.* Midwifery 2017; 51: 12–15. Available from: http://dx.doi.org/10.1016/j.midw.2017.05.005

118. Black LJ, Jacoby P, Allen KL, Trapp GS, Hart PH, Byrne SM et al. *Low vitamin D levels are associated with symptoms of depression in young adult males.* Aust. N. Z. J. Psychiatry 2014; 48(5): 464–471.

119. Huang JY, Arnold D, Qiu CF, Miller RS, Williams MA, Enquobahrie DA. *Association of serum vitamin D with symptoms of depression and anxiety in early pregnancy.* J. Womens Health 2014; 23(7): 588–595.

120. Bahramy P, Mohammad-Alizadeh-Charandabi S, Ramezani-Nardin F, Mirghafourvand M. *Serum levels of vitamin D, calcium, magnesium, and copper, and their relations with mental health and sexual function in pregnant Iranian adolescents.* Biol. Trace Elem. Res. 2020; 198(2): 440–448.

121. Lee van L, Cai S, Loy SL, Tham EKH, Yap FKP, Godfrey KM et al. *Relation of plasma tryptophan concentrations during pregnancy to maternal sleep and mental well-being: The GUSTO cohort.* J. Affect. Disord. 2018; 225: 523–529. Available from: http://dx.doi.org/10.1016/j.jad.2017.08.069

122. Trujillo J, Vieira MC, Lepsch J, Rebelo F, Poston L, Pasupathy D et al. *A systematic review of the associations between maternal nutritional biomarkers and depression and/or anxiety during pregnancy and postpartum.* J. Affect. Disord. 2018; 232: 185–203. Available from: https://doi.org/10.1016/j.jad.2018.02.004

123. Verly-Miguel MVB, Farias DR, Jesus Pereira Pinto de T, Lepsch J, Nardi AE, Kac G. *Serum docosahexaenoic acid (DHA) is inversely associated with anxiety disorders in early pregnancy.* J. Anxiety Disord. 2015; 30: 34–40. Available from: http://dx.doi.org/10.1016/j.janxdis.2014.12.002

124. van Lee L, Quah PL, Saw SM, Yap FKP, Godfrey KM, Chong YS et al. *Maternal choline status during pregnancy, but not that of betaine, is related to antenatal mental well-being: The growing up in Singapore toward healthy outcomes cohort.* Depress. Anxiety 2017; 34(10): 877–887.

125. Redpath N, Rackers HS, Kimmel MC. *The relationship between perinatal mental health and stress: A review of the microbiome.* Curr. Psychiatry Rep. 2019; 21(3): 18.

126. Rackers HS, Thomas S, Williamson K, Posey R, Kimmel MC. *Emerging literature in the microbiota-brain axis and perinatal mood and anxiety disorders.* Psychoneuroendocrinology 2018; 95: 86–96.

127. Hechler C, Borewicz K, Beijers R, Saccenti E, Riksen-Walraven M, Smidt H et al. *Association between psychosocial stress and fecal microbiota in pregnant women.* Sci. Rep. 2019; 9(1): 4463. Available from: http://dx.doi.org/10.1038/s41598-019-40434-8

128. Slykerman RF, Hood F, Wickens K, Thompson JMD, Barthow C, Murphy R et al. *Effect of lactobacillus rhamnosus HN001 in pregnancy on postpartum symptoms of depression and anxiety: A randomised double-blind placebo-controlled trial.* EBioMedicine 2017; 24: 159–165. Available from: https://doi.org/10.1016/j.ebiom.2017.09.013

129. Dawe JP, McCowan LME, Wilson J, Okesene-Gafa KAM, Serlachius AS. *Probiotics and maternal mental health: A randomised controlled trial among pregnant women with obesity.* Sci. Rep. 2020; 10(1): 1291. Available from: http://dx.doi.org/10.1038/s41598-020-58129-w

130. Hu J, Ly J, Zhang W, Huang Y, Glover V, Peter I et al. *Microbiota of newborn meconium is associated with maternal anxiety experienced during pregnancy.* Dev. Psychobiol. 2019; 61(5): 640–649.

131. Garza-Veloz I, Castruita-De La Rosa C, Ortiz-Castro Y, Flores-Morales V, Castañeda-Lopez ME, Cardenas-Vargas E et al. *Maternal distress and the development of hypertensive disorders of pregnancy.* J. Obstet. Gynaecol. (Lahore) 2017; 37(8): 1004–1008. Available from: https://doi.org/10.1080/01443615.2017.1313823

132. Avraham L, Tamar W, Eyal S, Gali P. *Perinatal outcomes and offspring long-term neuropsychiatric hospitalizations of mothers with anxiety disorder.* Arch. Womens Ment. Health 2020; 23(5): 681–688.

133. Ravid E, Salzer L, Arnon L, Eisner M, Wiznitzer A, Weller A et al. *Is there an association between maternal anxiety propensity and pregnancy outcomes?* BMC Pregnancy Childbirth 2018; 18(1): 22–24.

134. Rejnö G, Lundholm C, Öberg S, Lichtenstein P, Larsson H, D'Onofrio B et al. *Maternal anxiety, depression and asthma and adverse pregnancy outcomes – A population based study.* Sci. Rep. 2019; 9(1): 13101.

135. Bogaerts AFL, Van Den Bergh BRH, Witters I, Devlieger R. *Anxiety during early pregnancy predicts postpartum weight retention in obese mothers.* Obesity 2013; 21(9): 1942–1949.

136. Salehi-Pourmehr H, Niroomand S, Shakouri SK, Asgarlou Z, Farshbaf-Khalili A. *Association between antenatal and postpartum depression and anxiety with weight retention 1 year after childbirth: A longitudinal study.* Community Ment. Health J. 2018; 54(8): 1284–1294. Available from: http://dx.doi.org/10.1007/s10597-018-0324-y

137. Racine N, Plamondon A, Hentges R, Tough S, Madigan S. *Dynamic and bidirectional associations between maternal stress, anxiety, and social support: The critical role of partner and family support.* J. Affect. Disord. 2019; 252: 19–24. Available from: https://doi.org/10.1016/j.jad.2019.03.083

138. Brandão T, Brites R, Nunes O, Pires M, Hipólito J. *Anxiety and depressive symptoms during pregnancy, perceived control and posttraumatic stress symptoms after childbirth: A longitudinal mediation analysis.* J. Health Psychol. 2020; 25(13–14): 2085–2095.

139. Rwakarema M, Premji SS, Nyanza EC, Riziki P, Palacios-Derflingher L. *Antenatal depression is associated with pregnancy-related anxiety, partner relations, and wealth in women in Northern Tanzania: A cross-sectional study.* BMC Womens Health 2015; 15(1): 68. Available from: http://dx.doi.org/10.1186/s12905-015-0225-y

140. Grigoriadis S, Graves L, Peer M, Mamisashvili L, Tomlinson G, Vigod SN et al. *A systematic review and meta-analysis of the effects of antenatal anxiety on postpartum outcomes.* Arch. Womens Ment. Health 2019; 22(5): 543–556.

141. Dalke KB, Wenzel A, Kim DR. *Depression and anxiety during pregnancy: Evaluating the literature in support of clinical risk-benefit decision-making.* Curr. Psychiatry Rep. 2016; 18(6): 59. Available from: http://dx.doi.org/10.1007/s11920-016-0698-x

142. Kataja EL, Karlsson L, Huizink AC, Tolvanen M, Parsons C, Nolvi S et al. *Pregnancy-related anxiety and depressive symptoms are associated with visuospatial working memory errors during pregnancy.* J. Affect. Disord. 2017; 218: 66–74. Available from: http://dx.doi. org/10.1016/j.jad.2017.04.033

143. Stuebe AM, Meltzer-Brody S, Propper C, Pearson B, Beiler P, Elam M et al. *The mood, mother, and infant study: Associations between maternal mood in pregnancy and breastfeeding outcome.* Breastfeed Med. 2019; 14(8): 551–559.

144. Young-Wolff KC, Sarovar V, Tucker LY, Goler NC, Alexeeff SE, Ridout KK et al. *Association of depression, anxiety, and trauma with cannabis use during pregnancy.* JAMA Netw. Open 2020; 3(2): e1921333.

145. Gałazka I, Drosdzol-Cop A, Naworska B, Czajkowska M, Skrzypulec-Plinta V. *Does anxiety modify sexuality of pregnant women?* Ginekol. Pol. 2017; 88(12): 662–669.

146. Huizink AC, Menting B, De Moor MHM, Verhage ML, Kunseler FC, Schuengel C et al. *From prenatal anxiety to parenting stress: A longitudinal study.* Arch. Womens Ment. Health 2017; 20(5): 663–672.

147. Fairlie TG, Gillman MW, Rich-Edwards J. *High pregnancy-related anxiety and prenatal depressive symptoms as predictors of intention to breastfeed and breastfeeding initiation.* J. Womens Health (Larchmt.) Heal (San Fr.) 2009; 18(7): 945–953.

148. Hoff CE, Movva N, Rosen Vollmar AK, Pérez-Escamilla R. *Impact of maternal anxiety on breastfeeding outcomes: A systematic review.* Adv. Nutr. 2019; 10(5): 816–826.

149. Horsley K, Nguyen TV, Ditto B, Da Costa D. *The association between pregnancy-specific anxiety and exclusive breastfeeding status early in the postpartum period.* J. Hum. Lact. 2019; 35(4): 729–736.

150. Adedinsewo DA, Fleming AS, Steiner M, Meaney MJ, Girard AW. *Maternal anxiety and breastfeeding: Findings from the MAVAN (Maternal Adversity, Vulnerability and Neurodevelopment) study.* J. Hum. Lact. 2014; 30(1): 102–109.

151. Fallon V, Bennett KM, Harrold JA. *Prenatal anxiety and infant feeding outcomes: A systematic review.* J. Hum. Lact. 2016; 32(1): 53–66.

152. Hopkins J, Miller JL, Butler K, Gibson L, Hedrick L, Boyle DA. *The relation between social support, anxiety and distress symptoms and maternal fetal attachment.* J. Reprod. Infant. Psychol. 2018; 36(4): 381–392. Available from: http://doi.org/10.1080/02646838. 2018.1466385

153. Göbel A, Stuhrmann LY, Harder S, Schulte-Markwort M, Mudra S. *The association between maternal-fetal bonding and prenatal anxiety: An explanatory analysis and systematic review.* J. Affect. Disord. 2018; 239: 313–327.

154. Hernandez-Reif M, Kendrick A, Avery DM. *Pregnant women with depressive and anxiety symptoms read, talk, and sing less to their fetuses.* J. Affect. Disord. 2018; 229: 532–537. Available from: https://doi.org/10.1016/j.jad.2017.12.108

155. Hakanen H, Flykt M, Sinervä E, Nolvi S, Kataja EL, Pelto J et al. *How maternal pre – and postnatal symptoms of depression and anxiety affect early mother-infant interaction?* J. Affect. Disord. 2019; 257: 83–90. Available from: https://doi.org/10.1016/j.jad.2019.06.048

156. Nath S, Pearson RM, Moran P, Pawlby S, Molyneaux E, Challacombe FL et al. *The association between prenatal maternal anxiety disorders and postpartum perceived and observed mother-infant relationship quality.* J. Anxiety Disord. 2019; 68: 102148. Available from: https://doi.org/10.1016/j.janxdis.2019.102148

157. Dib EP, Padovani FHP, Perosa GB. *Mother-child interaction: Implications of chronic maternal anxiety and depression.* Psicol. Reflex. Crit. 2019; 32(1): 10.

158. Gelaye B, Sanchez SE, Andrade A, Gómez O, Coker AL, Dole N et al. *Association of antepartum depression, generalized anxiety, and posttraumatic stress disorder with infant birth weight and gestational age at delivery.* J. Affect. Disord. 2020; 262: 310–316.

159. Khalesi ZB, Bokaie M. *The association between pregnancy-specific anxiety and preterm birth: A cohort study.* Afr. Health Sci. 2018; 18(3): 569–575.

160. Pesonen AK, Lahti M, Kuusinen T, Tuovinen S, Villa P, Hämäläinen E et al. *Maternal prenatal positive affect, depressive and anxiety symptoms and birth outcomes: The PREDO study.* PLoS One 2016; 11(2): e0150058.

161. Vollrath ME, Sengpiel V, Landolt MA, Jacobsson B, Latal B. *Is maternal trait anxiety a risk factor for late preterm and early term deliveries?* BMC Pregnancy Childbirth 2016; 16(1): 286.

162. Gilles M, Otto H, Wolf IAC, Scharnholz B, Peus V, Schredl M et al. *Maternal hypothalamus-pituitary-adrenal (HPA) system activity and stress during pregnancy: Effects on gestational age and infant's anthropometric measures at birth.* Psychoneuroendocrinology 2018; 94: 152–161. Available from: https://doi.org/10.1016/j.psyneuen.2018.04.022

163. Dunkel Schetter C, Tanner L. *Anxiety, depression and stress in pregnancy: Implications for mothers, children, research, and practice.* Curr. Opin. Psychiatry 2012; 25(2): 141–148.

164. Doktorchik C, Premji S, Slater D, Williamson T, Tough S, Patten S. *Patterns of change in anxiety and depression during pregnancy predict preterm birth.* J. Affect. Disord. 2018; 227: 71–78. Available from: https://doi.org/10.1016/j.jad.2017.10.001

165. Weis KL, Walker KC, Chan W, Yuan TT, Lederman RP. *Risk of preterm birth and newborn low birthweight in military women with increased pregnancy-specific anxiety.* Mil. Med. 2020; 185(5–6): e678–e685.

166. Ding XX, Wu Y Le, Xu SJ, Zhu RP, Jia XM, Zhang SF et al. *Maternal anxiety during pregnancy and adverse birth outcomes: A systematic review and meta-analysis of prospective cohort studies.* J. Affect. Disord. 2014; 159(81): 103–110.

167. Sandman CA, Glynn L, Schetter CD, Wadhwa P, Garite T, Chicz-DeMet A et al. *Elevated maternal cortisol early in pregnancy predicts third trimester levels of placental corticotropin releasing hormone (CRH): Priming the placental clock.* Peptides 2006; 27(6): 1457–1463.

168. Hasanjanzadeh P, Faramarzi M. *Relationship between maternal general and specific-pregnancy stress, anxiety, and depression symptoms and pregnancy outcome.* J. Clin. Diagnostic Res. 2017; 11(4): VC04–7.

169. Ossola P, Ampollini P, Gerra ML, Tonna M, Viviani D, Marchesi C. *Anxiety, depression, and birth outcomes in a cohort of unmedicated women.* J. Matern. Fetal Neonatal Med. 2021; 34(10): 1606–1612. Available from: https://doi.org/10.1080/14767058.201 9.1641483

170. Keshavarzi F, Farnia V, Yazdchi K, Najafi F, Brand S, Bajoghli H et al. *Effect of maternal anxiety on maternal serum and fetal cord blood cortisol.* Asia Pac. Psychiatry 2014; 6(4): 435–439.

171. Smorti M, Ponti L, Tani F. *The effect of maternal depression and anxiety on labour and the well-being of the newborn.* J. Obstet. Gynaecol. (Lahore). 2019; 39(4): 492–497. Available from: https://doi.org/10.1080/01443615.2018.1536697

172. Hoyer J, Wieder G, Höfler M, Krause L, Wittchen HU, Martini J. *Do lifetime anxiety disorders (anxiety liability) and pregnancy-related anxiety predict complications during pregnancy and delivery?* Early Hum. Dev. 2020; 144: 105022. Available from: https://doi.org/10.1016/j.earlhumdev.2020.105022

173. Kaitz M, Mankuta D, Rokem AM, Faraone SV. *Moderate antenatal anxiety symptoms and birth outcomes of boys and girls.* J. Psychosom. Obstet. Gynecol. 2014; 35(4): 116–123.

174. Bayrampour H, Salmon C, Vinturache A, Tough S. *Effect of depressive and anxiety symptoms during pregnancy on risk of obstetric interventions.* J. Obstet. Gynaecol. Res. 2015; 41(7): 1040–1048.

175. Ogunyemi D, Jovanovski A, Liu J, Friedman P, Sugiyama N, Creps J et al. *The contribution of untreated and treated anxiety and depression to prenatal, intrapartum, and neonatal outcomes.* AJP Rep. 2018; 8(3): e146–57.

176. Sun Y, Huang K, Hu Y, Yan S, Xu Y, Zhu P et al. *Pregnancy-specific anxiety and elective cesarean section in primiparas: A cohort study in China.* PLoS One 2019; 14(5): e0216870.

177. Koelewijn JM, Sluijs AM, Vrijkotte TGM. *Possible relationship between general and pregnancy-related anxiety during the first half of pregnancy and the birth process: A prospective cohort study.* BMJ Open 2017; 7(5): e013413.

178. Capron LE, Ramchandani PG, Glover V. *Maternal prenatal stress and placental gene expression of NR3C1 and HSD11B2: The effects of maternal ethnicity.* Psychoneuroendocrinology 2018; 87: 166–172. Available from: http://dx.doi.org/10.1016/j.psyneuen.2017.10.019

179. Litzky JF, Deyssenroth MA, Everson TM, Lester BM, Lambertini L, Chen J et al. *Prenatal exposure to maternal depression and anxiety on imprinted gene expression in placenta and infant neurodevelopment and growth.* Pediatr. Res. 2018; 83(5): 1075–1083. Available from: http://dx.doi.org/10.1038/pr.2018.27

180. Mansell T, Novakovic B, Meyer B, Rzehak P, Vuillermin P, Ponsonby AL et al. *The effects of maternal anxiety during pregnancy on IGF2/H19 methylation in cord blood.* Transl. Psychiatry 2016; 6(3): e765–767. Available from: http://dx.doi.org/10.1038/tp.2016.32

181. Ramos IF, Guardino CM, Mansolf M, Glynn LM, Sandman CA, Hobel CJ et al. *Pregnancy anxiety predicts shorter gestation in Latina and non-Latina white women: The role of placental corticotrophin-releasing hormone.* Psychoneuroendocrinology 2019; 99: 166–173. Available from: https://doi.org/10.1016/j.psyneuen.2018.09.008

182. Vangeel EB, Pishva E, Hompes T, Hove van den D, Lambrechts D, Allegaert K et al. *Newborn genome-wide DNA methylation in association with pregnancy anxiety reveals a potential role for GABBR1.* Clin. Epigenetics 2017; 9(1): 107.

183. Pinheiro KAT, Pinheiro RT, Coelho FMDC, Da Silva RA, Quevedo LÁ, Schwanz CC et al. *Serum NGF, BDNF and IL-6 levels in postpartum mothers as predictors of infant development: The influence of affective disorders.* PLoS One 2014; 9(4): e94581.

184. Gur TL, Shay L, Palkar AV, Fisher S, Varaljay VA, Dowd S et al. *Prenatal stress affects placental cytokines and neurotrophins, commensal microbes, and anxiety-like behavior in adult female offspring.* Brain Behav. Immun. 2017; 64: 50–58. Available from: http://dx.doi. org/10.1016/j.bbi.2016.12.021

185. Uguz F, Sonmez EO, Sahingoz M, Gokmen Z, Basaran M, Gezginc K et al. *Maternal generalized anxiety disorder during pregnancy and fetal brain development: A comparative study on cord blood brain-derived neurotrophic factor levels.* J. Psychosom. Res. 2013; 75(4): 346–350. Available from: http://dx.doi.org/10.1016/j.jpsychores.2013.04.010

186. Glover V, O'Connor TG, O'Donnell K. *Prenatal stress and the programming of the HPA axis.* Neurosci. Biobehav. Rev. 2010; 35(1): 17–22. Available from: http://dx.doi.org/10.1016/j.neubiorev.2009.11.008

187. Romero-Gonzalez B, Caparros-Gonzalez RA, Gonzalez-Perez R, Delgado-Puertas P, Peralta-Ramirez MI. *Newborn infants' hair cortisol levels reflect chronic maternal stress during pregnancy.* PLoS One 2018; 13(7): e0200279.

188. van der Voorn B, Hollanders JJ, Kieviet N, Dolman KM, De Rijke YB, Van Rossum EFC et al. *Maternal stress during pregnancy is associated with decreased cortisol and cortisone levels in neonatal hair.* Horm. Res. Paediatr. 2019; 90(5): 299–307.

189. Adamson B, Letourneau N, Lebel C. *Prenatal maternal anxiety and children's brain structure and function: A systematic review of neuroimaging studies.* J. Affect. Disord. 2018; 241: 117–126. Available from: https://doi.org/10.1016/j.jad.2018.08.029

190. Dean DC, Planalp EM, Wooten W, Kecskemeti SR, Adluru N, Schmidt CK et al. *Association of prenatal maternal depression and anxiety symptoms with infant white matter microstructure.* JAMA Pediatr. 2018; 172(10): 973–981.

191. Qiu A, Rifkin-Graboi A, Chen H, Chong YS, Kwek K, Gluckman PD et al. *Maternal anxiety and infants' hippocampal development: Timing matters.* Transl. Psychiatry 2013; 3(9): e306–307. Available from: http://dx.doi.org/10.1038/tp.2013.79

192. Wu Y, Lu YC, Jacobs M, Pradhan S, Kapse K, Zhao L et al. *Association of prenatal maternal psychological distress with fetal brain growth, metabolism, and cortical maturation.* JAMA Netw. Open 2020; 3(1): e1919940.

193. Acosta H, Tuulari JJ, Scheinin NM, Hashempour N, Rajasilta O, Lavonius TI et al. *Maternal pregnancy-related anxiety is associated with sexually dimorphic alterations in amygdala volume in 4-year-old children.* Front. Behav. Neurosci. 2019; 13: 175.

194. Marečková K, Mareček R, Bencurova P, Klánová J, Dušek L, Brázdil M. *Perinatal stress and human hippocampal volume: Findings from typically developing young adults.* Sci. Rep. 2018; 8(1): 4696.

195. Bekkhus M, Lee Y, Nordhagen R, Magnus P, Samuelsen SO, Borge AIH. *Re-examining the link between prenatal maternal anxiety and child emotional difficulties, using a sibling design.* Int. J. Epidemiol. 2018; 47(1): 156–165.

196. Korja R, Nolvi S, Grant KA, McMahon C. *The relations between maternal prenatal anxiety or stress and child's early negative reactivity or self-regulation: A systematic review.* Child Psychiatry Hum. Dev. 2017; 48(6): 851–869.

197. Mughal MK, Giallo R, Arnold P, Benzies K, Kehler H, Bright K et al. *Trajectories of maternal stress and anxiety from pregnancy to three years and child development at 3 years of age: Findings from the All Our Families (AOF) pregnancy cohort.* J. Affect. Disord. 2018; 234: 318–326. Available from: https://doi.org/10.1016/j.jad.2018.02.095

198. Tan HK, Goh SKY, Tsotsi S, Bruntraeger M, Chen HY, Broekman B et al. *Maternal antenatal anxiety and electrophysiological functioning amongst a sub-set of preschoolers participating in the GUSTO cohort.* BMC Psychiatry 2020; 20(1): 62.

199. Tarabulsy GM, Pearson J, Vaillancourt-Morel MP, Bussières EL, Madigan S, Lemelin JP et al. *Meta-analytic findings of the relation between maternal prenatal stress and anxiety and child cognitive outcome.* J. Dev. Behav. Pediatr. 2014; 35(1): 38–43.

200. Maria A, Nissilä I, Shekhar S, Kotilahti K, Tuulari JJ, Hirvi P et al. *Relationship between maternal pregnancy-related anxiety and infant brain responses to emotional speech – A pilot study.* J. Affect. Disord. 2020; 262: 62–70. Available from: https://doi.org/10.1016/j.jad.2019.10.047

201. Mughal MK, Giallo R, Arnold PD, Kehler H, Bright K, Benzies K et al. *Trajectories of maternal distress and risk of child developmental delays: Findings from the All Our Families (AOF) pregnancy cohort.* J. Affect. Disord. 2019; 248: 1–12. Available from: https://doi.org/10.1016/j.jad.2018.12.132

202. Polte C, Junge C, Soest von T, Seidler A, Eberhard-Gran M, Garthus-Niegel S. *Impact of maternal perinatal anxiety on social-emotional development of 2-year-olds, a prospective study of Norwegian mothers and their offspring: The impact of perinatal anxiety on child development.* Matern. Child Health J. 2019; 23(3): 386–396. Available from: http://dx.doi.org/10.1007/s10995-018-2684-x

203. Brannigan R, Cannon M, Tanskanen A, Huttunen MO, Leacy FP, Clarke MC. *The association between subjective maternal stress during pregnancy and offspring clinically diagnosed psychiatric disorders.* Acta Psychiatr. Scand. 2019; 139(4): 304–310.

204. Hentges RF, Graham SA, Plamondon A, Tough S, Madigan S. *A developmental cascade from prenatal stress to child internalizing and externalizing problems.* J. Pediatr. Psychol. 2019; 44(9): 1057–1067.

205. Peltola MJ, Mäkelä T, Paavonen EJ, Vierikko E, Saarenpää-Heikkilä O, Paunio T et al. *Respiratory sinus arrhythmia moderates the impact of maternal prenatal anxiety on infant negative affectivity.* Dev. Psychobiol. 2017; 59(2): 209–216.

206. Madigan S, Oatley H, Racine N, Fearon RMP, Schumacher L, Akbari E et al. *A meta-analysis of maternal prenatal depression and anxiety on child socioemotional development.* J. Am. Acad. Child Adolesc. Psychiatry 2018; 57(9): 645–657.e8. Available from: https://doi.org/10.1016/j.jaac.2018.06.012

207. Thiel F, Iffland L, Drozd F, Haga SM, Martini J, Weidner K et al. *Specific relations of dimensional anxiety and manifest anxiety disorders during pregnancy with difficult early infant temperament: A longitudinal cohort study.* Arch. Womens Ment. Health 2020; 23(4): 535–546.

208. Bolea-Alamañac B, Davies SJC, Evans J, Joinson C, Pearson R, Skapinakis P et al. *Does maternal somatic anxiety in pregnancy predispose children to hyperactivity?* Eur. Child Adolesc. Psychiatry 2019; 28(11): 1475–1486. Available from: https://doi.org/10.1007/s00787-019-01289-6

209. Vizzini L, Popovic M, Zugna D, Vitiello B, Trevisan M, Pizzi C et al. *Maternal anxiety, depression and sleep disorders before and during pregnancy, and preschool ADHD symptoms in the NINFEA birth cohort study.* Epidemiol. Psychiatr. Sci. 2019; 28(5): 521–531.

210. Auger N, Low N, Lee GE, Ayoub A, Luu TM. *Maternal stress and anxiety disorders and the longitudinal risk of fractures in children.* Bone 2020; 130: 115143. Available from: https:// doi.org/10.1016/j.bone.2019.115143

211. Fan F, Zou Y, Tian H, Zhang Y, Zhang J, Ma X et al. *Effects of maternal anxiety and depression during pregnancy in Chinese women on children's heart rate and blood pressure response to stress.* J. Hum. Hypertens. 2016; 30(3): 171–176.

212. Silva CCV, Vehmeijer FOL, El Marroun H, Felix JF, Jaddoe VWV, Santos S. *Maternal psychological distress during pregnancy and childhood cardio-metabolic risk factors.* Nutr. Metab. Cardiovasc. Dis. 2019; 29(6): 572–579. Available from: https://doi.org/10.1016/j.numecd.2019.02.008

213. Krause L, Einsle F, Petzoldt J, Wittchen HU, Martini J. *The role of maternal anxiety and depressive disorders prior to and during pregnancy and perinatal psychopathological symptoms for early infant diseases and drug administration.* Early Hum. Dev. 2017; 109: 7–14. Available from: http://dx.doi.org/10.1016/j.earlhumdev.2017.03.009

214. Teyhan A, Galobardes B, Henderson J. *Child allergic symptoms and mental well-being: The role of maternal anxiety and depression.* J. Pediatr. 2014; 165(3): 592–599.e5. Available from: http://dx.doi.org/10.1016/j.jpeds.2014.05.023

215. Brew BK, Lundholm C, Viktorin A, Lichtenstein P, Larsson H, Almqvist C. *Longitudinal depression or anxiety in mothers and offspring asthma: A Swedish population-based study.* Int. J. Epidemiol. 2018; 47(1): 166–174.

216. Zijlmans MAC, Beijers R, Riksen-Walraven MJ, de Weerth C. *Maternal late pregnancy anxiety and stress is associated with children's health: A longitudinal study.* Stress 2017; 20(5): 495–504. Available from: https://doi.org/10.1080/10253890.2017.1348497

217. Bauer A, Knapp M, Parsonage M. *Lifetime costs of perinatal anxiety and depression.* J. Affect. Disord. 2016; 192: 83–90. Available from: http://dx.doi.org/10.1016/j.jad.2015.12.005

218. Smith T, Gemmill AW, Milgrom J. *Perinatal anxiety and depression: Awareness and attitudes in Australia.* Int. J. Soc. Psychiatry 2019; 65(5): 378–387.

219. Ford E, Shakespeare J, Elias F, Ayers S. *Recognition and management of perinatal depression and anxiety by general practitioners: A systematic review.* Fam. Pract. 2017; 34(1): 11–19.

220. Chan CY, Lee AM, Koh YW, Lam SK, Lee CP, Leung KY et al. *Associations of body dissatisfaction with anxiety and depression in the pregnancy and postpartum periods: A longitudinal study.* J. Affect. Disord. 2020; 263: 582–592. Available from: https://doi.org/10.1016/j.jad.2019.11.032

221. Arch JJ. *Pregnancy-specific anxiety: Which women are highest and what are the alcohol-related risks?* Compr. Psychiatry 2013; 54(3): 217–228. Available from: http://dx.doi.org/10.1016/j.comppsych.2012.07.010

222. Salih Joelsson L, Tydén T, Wanggren K, Georgakis MK, Stern J, Berglund A et al. *Anxiety and depression symptoms among sub-fertile women, women pregnant after infertility treatment, and naturally pregnant women.* Eur. Psychiatry 2017; 45: 212–219.

223. Watson SJ, Lewis AJ, Boyce P, Galbally M. *Exercise frequency and maternal mental health: Parallel process modelling across the perinatal period in an Australian pregnancy cohort.* J. Psychosom. Res. 2018; 111(May): 91–99. Available from: https://doi.org/10.1016/j.jpsychores.2018.05.013

Address: Agata Mikołajków
Wroclaw Medical University
50-367 Wrocław, Wybrzeże L. Pasteura Street 10
e-mail: mikolajkowagata@gmail.com