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Review Article

Correlation between postpartum depression and omega-3, micronutrients

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ABSTRACT

In recent years, attention has been called to the link between nutrition and mental health. Postpartum depression is an important depressive disorder which often arises 6 to 12 weeks after giving birth and can happen at any time within one year. Postpartum depression prevalence is around 20% worldwide. Genetic predisposition and environmental factors, as well as certain social, psychological and biological factors constitute risk factors for postpartum depression. While malnutrition is among the biological factors, there is a correlation between nutrients such as folic acid, vitamin B_{12}, vitamin D, iron, selenium, zinc, and n-3 fatty acids and psychological state. The nutrients that claim most attention relating to postpartum depression are n-3 essential fatty acids. Insufficient intake of n-3, folic acid, vitamins B and iron is observed in pregnant women. Failing to meet the needs of the mother due to malnutrition during pregnancy can increase the risk of depleting the body's nutrient reserves and developing postpartum. This risk factor needs to be kept in check by determining and keeping track of the nutrient needs of the mother during the perinatal period.

Keywords: Depression, Mineral, Omega-3, Postpartum, Vitamin

INTRODUCTION

Depression is a syndrome involving the slowing down of thoughts and actions in a mood of deep sadness, decreased energy, feelings of worthlessness and low self-esteem, weakness, lethargy, pessimism and finally emotions and thoughts like suicide.[1] It is also major public health issue which afflicts women in their childbearing years twice as often as men.

Postpartum depression (PPD) is an important depressive disorder which often arises 6 to 12 weeks after giving birth and can happen at any time within one year.[2] According to DSM-5, postpartum depression is defined as a subgroup of major depressive disorder (MDD) with an onset within 4 months of giving birth.[3] According to World Health Organization's data, 10% of pregnant women across the world can experience mental illness with underlying depression following giving birth.

In developing countries, this ratio is 15.6% during pregnancy and 19.8% following giving birth. In cases of acute depression, the distress experienced by mothers can be severe enough to result in suicide. The growth and development of the babies are also adversely affected by the fact that mothers who experience depression following giving birth cannot adequately provide child care.[4] Mothers who develop postpartum depression are twice as likely to experience recurrent depression in the next five years.[5]

Postpartum depression may involve any one or more of the symptomatic characteristics of depressive disorder including low mood, deep sorrow, poor concentration, and loss of appetite. Neglect of the baby can also be present. Further symptoms may include growing concerns regarding parental role, feelings of inadequacy or fears regarding the baby's health.[3,6]

A general anxiety inventory like the State-Trait Anxiety Inventory (STAI) was commonly used measure signs of anxiety in women during pregnancy and following giving birth.[7] Edinburgh Postnatal Depression Scale (EPDS) was later developed, because scales designed to screen for depression or to diagnose general depressive disorders did not take into account the atypicality of the disorder. Today, EPDS is considered the gold standard in this field.[3]

Children of depressed mothers experience behavioural and developmental problems, higher risk in development, as well as delays in cognitive and emotional development. It becomes harder to monitor and to treat this disease, because women often neglect PPD symptoms.[8] It is essential to take preventive measures by defining whether postpartum depression is a separate type of depression and time of detection as well as factors related to prepartum depression. From an etiological point of view, depressive disorders are a heterogeneous group and make up the last stage of many different causal pathways.[9]

Depression or anxiety experienced during pregnancy, stress, low social support and history of depression are among major causes of postpartum depression. The stress of taking care of a new-born, low self-esteem, maternal neuroticism, a difficult baby, obstetrical and pregnancy complications, negative cognitive qualities, poor relationship with husband and low socioeconomic status can also be listed among causes.[10]

Evidence about the role of nutrition in mental health date back to ancient times. Hippocrates said, "Leave your drugs in the chemist's pot, if you can heal the patient with food." in 400 B.C. Twenty first century medical literature reports improvements in irritability and other mood related symptoms, as well as in mental disorders after patients suffering from malnutrition are treated with minerals.[11]

Studies have long been conducted regarding the link between nutrition and brain function. There are reports of a credible link between mood and nutrients such as folic acid, vitamin D, vitamin B_{12}, iron, selenium, zinc and polyunsaturated fatty acids (PUFAs).[2]

Kaplan et al have discovered potential beneficial effects of vitamins (mostly B, but also C, D and E), minerals (calcium, chromium, iron, magnesium, zinc and selenium), and vitamin-like compounds (choline) on mood symptoms.[11] This compilation is aimed at exploring the correlation between various nutrients and postpartum depression, as well as improving nutritional preventive measures.

THE CORRELATION BETWEEN VARIOUS NUTRIENTS AND POSTPARTUM DEPRESSION

Omega-3 fatty acid

Where people used to consume equal amounts of omega-3 (n-3) and omega-6 (n-6) fatty acids, today the ratio of n-3:n-6 fatty acids in the American diet is estimated as 1:10. This dramatic drop in n-3 fatty acid consumption in many countries is believed to impact the prevalence of all diseases and pregnancy results.[12] Phospholipids make up 60% of the brain's dry weight. Half of this is n-6 (arachidonic acid) and the other half is n-3 and docosahexaenoic acid (DHA). Phospholipids are essential for neuron functions, especially synaptic structure. Dopamine, serotonin, glutamate and acetylcholine also play an important role in signal transmission.[12,13] Omega-3 fatty acids can be effective in decreasing the severity of major depressive episodes by regulating the overactivity of T cells and antiphospholipid antibodies. Inflammatory mechanisms can affect neurotransmitter levels especially by reducing serotonin levels. Omega-3 fatty acids can lessen the severity of depression by improving serotonin production.[13] n-3 polyunsaturated fatty acid (PUFA) levels in cell tissue (red blood cell membrane, plasma, etc.) content of patients with depression as well as in their dietary intake was reported as being significantly low.14 Major depression is linked to changes in the fatty acid composition of serum lipids. A decrease in n-3 fatty acids and an increase in serum n-6/n-3 PUFA ratio in has been observed in patients with depression. Increased n-6/n-3 ratio can be related to increased proinflammatory cytokines and eicosanoids seen in major depression.15 Incidence of depression is reported as lower in populations where daily intake of omega-3 fatty acids is higher in comparison to populations with lower intake.[16] Hibbeln has discovered a significant inverse relationship between fish and seafood consumption of countries and prevalence of postpartum depression.[17] Due to high concentrations of DHA in the brain cell membrane lipids, developing fetus consumes large amounts of maternal DHA following fertilization. This is why maternal DHA reserves (22:6 n-3) are gradually depleted in the late stages of pregnancy and early stages following birth. Low levels of DHA in the brain can contribute to developing postpartum depression.[9,18] Llorente et al gave nursing mothers 200 mg/day of DHA supplements for 4 weeks following birth and later assessed them based on their DHA levels as well as Edinburgh Postnatal Depression scale and Beck Depression Inventory.[18] 4 weeks after birth, the DHA levels in serum of the group that used DHA had a rise in DHA levels, while the control group had a drop. However, no difference was observed between the two groups in terms of depression scale scores. It was reported that using n-3 fatty acid between weeks 34 and 36 of pregnancy alone had no preventive

effect on postpartum depression in patients with a history of depression.[19] A major source of the 300 mg/day of DHA which is recommended during pregnancy and lactation is fatty cold-water fish. Consuming 2 to 3 portions of deep sea fish from clean waters weekly during pregnancy is enough to meet the DHA requirement. Other foods high in DHA for pregnant and nursing mothers are n-3 enriched eggs and DHA supplements. Vegetable sources for n-3 are flaxseed and nuts, especially walnut and walnut oil, but these convert to DHA at a lower rate.[12] Sweden and FAO/WHO emphasize the importance of the link between fish and seafood and mental health and pregnancy.[9]

Vitamin D

Vitamin D is biologically inert until it is metabolized in the liver. It first needs to be converted into 25-hydroxyvitamin D (25-OH D3) in the liver and then into 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) in the kidneys. This form of vitamin D is later bound to vitamin D receptors (VDR) in order to regulate cellular function in many types of tissue including brain neurons.[20] In an adult human brain, vitamin D receptors (VDR) and 1α-hydroxylase enzymes which are required for 1,25(OH)2D3 production in the neuronal and glial cells are found. The increase in the amount of VDR and 1α-hydroxylase which are responsible for active vitamin production in the human brain, leads to the notion that vitamin D is important in mental processes.[21]

Even though the mechanism of action of low concentrations of vitamin D on developing depression has not yet been established, its deficiency fails to stimulate the vitamin D receptors leading to a breakdown of the hormonal processes in the brain which serve to prevent mood disorders.[22] Mood disorders (premenstrual syndrome, seasonal affective disorder, mood disorder and major depressive disorder, etc.) are reported to have a significant connection with low serum 25-OH D3 levels.[23] Vitamin D deficiency (25-OH D3 <32 ng/mL) is an epidemic affecting 75% of women of childbearing age.[24] Maternal vitamin D deficiency is common during pregnancy and even with vitamin D supplements vitamin D is sufficient in only a small percentage of women and babies.[25]

Low levels of vitamin D can be overlooked as a risk factor for PPD. High prevalence of maternal vitamin D deficiency (vitamin D levels of 25-50 nmol/L) during pregnancy and following giving birth were indicated in various populations at different latitudes as 5 to 20% in populations with fair skin and 30 to 70% in populations with dark skin or wearing hijab. In fact, vitamin D deficiency is endemic in some populations.[25,26] Taking into account the high percentage of vitamin D deficiency seen in pregnant women along with prevalence of PPD lends itself to the notion that the link between vitamin D deficiency and PPD play an important role on public health. In a study done to shed a light on the effect of vitamin D deficiency on the occurrence of PPD, a significant correlation between low levels of 25-OH D3 over time, which is a sign of postpartum depression, and high EPDS scores was discovered.[24] Postpartum depression was most often seen in winter months.[27,28] In a study, Fu et al have found serum 25-OH D3 levels in women without PPD higher that in women suffering from postpartum depression.[25] A prospective study has discovered a negative correlation between prenatal vitamin D levels at week 18 of gestation and PPD symptoms.[29] Lamb et al have reported that women with vitamin D deficiency during early and late term pregnancy and after giving birth showed significantly more signs of depression.[30] While the study by Nielsen et al discovered no general correlation between vitamin D status during pregnancy and risk of PPD.[31] Among factors known to affect blood 25-OH D3 levels are; race, vitamin D intake, length of exposure to sunlight, amount of adipose tissue, age and level of physical activity. It is difficult to assess the risk of encountering clinical or biochemical results of vitamin D deficiency solely based on 25-OH D3 concentrations. Duration of vitamin D deficiency, reaction of the vitamin D receptors, dietary calcium intake, and individual calcium requirements alter the clinical results of vitamin D deficiency. Being exposed to sunlight and time spent outdoors has a larger effect on serum 25-OH D3 levels than dietary vitamin D intake.[32]

Folic acid - Vitamin B_{12} - Vitamin B6

In case of folic acid and B_{12} deficiency similarities are clear in the clinical picture based on their metabolic relationship. Folic acid and B_{12} metabolism is joined by a single central biochemical reaction, namely the methylation of homocysteine, which is catalyzed by methionine synthase to methionine. Decrease in methionine synthase activity and rise in homocysteine can have serious consequences. High levels of homocysteine is toxic for not only vascular endothelial cells, but also for neuronal cells.[33] Increased plasma homocysteine is a functional sign of folate deficiency and homocysteine levels are high in depressive patients.[34] A biochemical and in vitro study has shown that low folic acid levels are linked to depression in the general population and that folic acid deficiency increases risk of depression.[35-37] Some studies have discovered low levels of serum or red blood cell folic acid concentrations in patients with major depression. Folic acid is an important part of the single carbon metabolism which forms S-Adenosyl Methionine (SAM). S-Adenosyl Methionine provides methyl groups vital to neurological function.[34,36] Similarly, deficiency of vitamins B_{12} and B_6 is linked to hyperhomocysteinemia.[38] In theory, vitamin B_6 deficiency can cause depression, because it is a cofactor in the tryptophan serotonin pathway.[39] Vitamin B_{12} is a cofactor in the formation of S-Adenosyl Methionine which is a product in the production of neurotransmitters.[40] Myake et al have found no quantifiable correlation between folic acid, cobalamin or

pyridoxine intake and risk of postpartum depression in women who developed depression 2 to 9 months postpartum at a rate of 14.0%.[41] Folic acid status before and during pregnancy, as well as folic acid and vitamins B_{12} and B_6 intake in diet have been reported to have no link to postpartum depression symptoms.[38] Kendrick et al, based on findings of the Southampton Women's Survey (SWS), have determined that depressive symptoms listed on GP records of women of childbearing age over two years have no correlation to red blood cell folic acid concentration.[42] GUSTO study by Chong et al has determined that plasma vitamin B_{12} concentrations have no correlation to perinatal depression and although low plasma folic acid status during pregnancy is linked to antenatal depression, it has no correlation to postnatal depression.[43]

Zinc

Zinc (Zn), which is found in large concentrations in the brain, is essential for nerve conduction, DNA replication and transcription, protein synthesis, stabilization of cell membranes and regulation of the immune system. It is also an essential mineral for hundreds of enzymes in the body.[44,45] In case of zinc deficiency, neuronal function can be affected due to oxidative stress on the neuronal cells.[46] Low Zn levels have been associated with mood disorders since the 1980's.[47] While the hypothesis that a general Zn deficiency is present in depressive disorders has not been corroborated, Zn concentrations differ based on accompanying disorders and severity of depression.[48] In a study by Wójcik et al, a negative correlation was discovered between serum zinc levels measured on the third and 30th days following giving birth and the scores on the Edinburgh Postnatal Depression Scale (EPDS).[49] While the EPDS score on the third day following giving birth is significantly higher (45%) than on the 30th day, serum zinc concentration was found to be 24% lower. Even though zinc supplements prove beneficial in antidepressant treatment, no decrease is reported in the average score of depressive symptoms 8 weeks after giving birth in spite of zinc supplements.[50,51]

Iron

Iron deficiency is the most common nutrient deficiency in the world and it is seen in 50% of women especially of childbearing age.[52] In developed countries, prevalence of iron deficiency during pregnancy is between 18 and 40%. Iron deficiency has adverse effects on areas of women's mental health such as mood, short term memory, verbal learning, attention span/concentration, and intelligence. It can also cause depression.[52,53] The general population has been divided into three groups based on severity of iron deficiency. Depletion of iron reserves; normal iron dependent protein production and depleted iron reserves with normal hemoglobin concentrations (ferritin <12 µg/L) exist.[2] Marginal iron deficiency; depleted iron reserves, decreased iron dependent protein production (eg. oxidative enzymes) and normal hemoglobin concentrations (transferrin saturation <16-20%). Iron deficiency anemia; characterized by depleted iron reserves, decreased haemoglobin concentrations and decreased iron-oxidative enzymes.[54,55] Iron is an important micronutrient for oxidative metabolism, cellular immune response and erythropoiesis.[56] Iron requirement increases in the second trimester of pregnancy and iron reserves are depleted.[57] In the early postpartum period, women afflicted with anaemia can run a higher risk of developing PPD.[58] Albacar et al have evaluated depressive symptoms at postpartum 48 hours, 8 weeks and 32 weeks with relation to iron storage parameters (ferritin, transferrin, free iron and transferrin saturation) in blood sample taken 48 hours after giving birth and have discovered a strong correlation between ferritin and PPD.[55] Furthermore, the role of iron in etiology of PPD and use of ferritin as indicated by iron deficiency in the postpartum period is corroborated. In another randomized, double blind, placebo-controlled study on 70 mothers suffering from postpartum depression, mothers were divided into two groups; one group receiving iron treatment (50 mg elemental iron/day) one week after giving birth and the other receiving a placebo. After six weeks, the improvement in PPD symptoms in both groups were compared. Early iron supplement in mothers with postpartum depression significantly restored iron reserves and led to notable improvement in PPD with a 42.8% healing rate over 6 weeks. In mothers who were not treated with iron, ongoing PPD is thought to be linked to low postpartum ferritin levels.[59] In yet another study, no difference was discovered between EPDS scores of anaemic and nonanemic mothers regardless of the timing of the evaluation, whereas iron levels of women with possible postpartum depression and of those without were found to be similar. This is why no correlation is supported between maternal iron status and postpartum depression.[60]

Selenium

Total body selenium content in adult humans varies between countries because dietary intake of this element changes due to the differences in the geographical distribution of selenium content in soil.[61] Selenium is believed to play an important role in brain function since it metabolizes so uniquely in the brain. The mechanism through which selenium affects mood is unclear. However, small changes in thyroid functions are correlated to depressive symptoms.[62] Selenium has important modulating effects on dopamine and dopamine plays a role in the pathophysiology of depression and other psychiatric diseases.[63] While reduced levels of selenium in the brain are linked to cognitive impairment.[64] Some studies have revealed that serum selenium concentrations decreased throughout pregnancy edir.[65,66] In a study by Mokheber et al, selenium supplement resulted in a notable increase in average serum selenium concentration and average EPDS score was significantly lower.[67] These findings support the

notion that selenium supplement during pregnancy can be an effective approach in preventing postpartum depression.

Magnesium

Magnesium is the fourth most abundant trace element in the human body.[68] Magnesium deficiency is reported in cases of depression. Magnesium is a natural calcium channel blocker and is needed for relaxation. Calcium stimulates the nerves and magnesium calms them down. It is maintained that all these systems are confused in the pathophysiology of depression, that calcium or magnesium deficiency can increase susceptibility to anxiety and panic and that low Mg/Ca ratio can trigger a stress response.[53,69]

During pregnancy, the foetus and the placenta transports large amounts of magnesium especially from the mother. In cases where the mother's magnesium intake is insufficient, this depletion of magnesium is considered the cause of postpartum depression. Lactation is also known to deplete maternal magnesium.[70] Although high magnesium intake in diet was found to be linked to fewer depression symptoms in a systematic compilation, the need for further research on this topic is indicated.[71] Fard et al have found no decrease in depressive symptoms 8 weeks after giving birth in spite of 8 weeks of magnesium supplementation.[51]

CONCLUSION

A nutritional program which fulfils dietary requirements during pregnancy is crucial for the health of the mother and the foetus. Recognizing the factors of postpartum depression related to nutrition is crucial for taking preventive measures. The depletion of the mother's nutrient reserves and the failure to meet her dietary requirements can increase the risk of postpartum maternal depression. A strong correlation between low n-3 PUFA consumption and developing postpartum depression is recognized.

This is why the 300 mg/day dietary requirement for DHA can be met by consuming 1 to 2 portions of cold sea fish. Again, deficiency of B vitamins results in anaemia, peripheral neuropathy and acute psychological disorders. Sufficient blood levels of vitamin D and ferritin during and after pregnancy plays a major role in preventing depression. Medical care during pregnancy should not only monitor the mother's weight gain, but also assess whether her increasing nutrient requirements are adequately met. Nutritional advice should be affordable, safe, easy to implement and generally acceptable for patients. Although studies have been done on the important role of omega 3 fatty acids and certain micronutrients on preventing postpartum depression, further research is required to definitively address their effects on postpartum depression.

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