

The Role of Essential Fatty Acids Supplementation on the Treatment of Prenatal Depression

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Abstract

Prenatal depression is a complex disorder which could cause undesirable impacts to both mothers and offspring. Majority of the cases are often undertreated and the most common treatment, selective serotonin reuptake inhibitor (SSRI), still faced a lot of dilemma due to its effect on fetus' development. Studies have shown that low level essential fatty acids, especially omega-3 fatty acids are associated with depressive symptom during pregnancy ad it has been widely known that supplementation of omega-3 fatty acids is required for healthy pregnancy. Through this essay, I would like to investigate the role of essential fatty acids supplementation during prenatal depression. In these past years, several intervention studies have been conducted to test the efficacy of omega-3 fatty acids on prenatal depression treatment and yielded mix results. Therefore, the role of omega-3 fatty acids supplementation on prenatal depression treatment is still inconclusive. Future investigations are promising as omega-3 fatty acids have roles in monoaminergic transmission and its supplementations are safe and even suggested during pregnancy.

Keywords: prenatal depression, depression, essential fatty acids, pregnancy

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Introduction

Prenatal maternal depression is known to have long-term effects on development and physiological function of the offsprings. Both animal and human studies have displayed that prenatal depression could affect physical and mental health outcomes of the offsprings. Prenatal depression itself is a complex and multifactorial mood disorder as it may be caused by several causes and has multiple pathophysiologies [1]. One of the factors that may contribute to prenatal depression is inadequate dietary intake during gestations. An association was shown between nutrition and prenatal depression where higher depressive symptoms during pregnancies were related to lower intake of healthy nutrition and higher levels of unhealthy nutrition [2]. Deficiency of specific nutrients were also linked to prenatal depression such as iron [3], zinc [4] and particularly, essential fatty acid [5]. Several studies confirmed the importance of essential fatty acid for a healthy pregnancy; however the role of this specific nutrient in prenatal depression is still poorly understood. Therefore, in this essay I would like to investigate the role that essential fatty acids have during prenatal depression. First, prenatal depression will extensively be explained and then, a review on the importance of essential fatty acids in a healthy pregnancy will be given. Lastly, I will discuss several findings from intervention trials of fatty acids supplementation during pregnancy and its effect on prenatal maternal depression. This study literature is crucial to examine the role of essential fatty acids supplementation on the treatment of depression in pregnant women.

Prenatal depression

Prenatal depression refers to one form of depression that could affect women during pregnancy period, and has been shown to be prevalent among pregnant women [6],[7]. In fact, it affects around 15% in the developed world and approximately 20-40 % in developing countries [8]. Although the prevalence is moderately high, the majority of these cases are untreated and undiagnosed [9] which may then increase the risk of depression for the mother later in life [10]. Prenatal depression does not only negatively affect the mother's life, but also has detrimental effects towards the child's development. Several studies in animal model have shown that exposure at pregnant animal to stressful events resulted in disturbance of growth [11],sexual maturation [12] , motor development [13], and immune function [14] of the offsprings. In human, prenatal depression impacted prenatal health outcomes, such as the risk of preterm birth [15] and fetal growth restriction [16], and also physical and mental health outcomes of the offsprings [17].

Studies were done to identify risk factors that may influence prenatal depression, and some findings showed that genetic and environmental factors might play roles in prenatal depression. The genetics of depression has been studied extensively in the past years since depression is a moderately heritable disorder with a heritability of approximately 40% assessed in female twins [18]. However, the results of genetic studies of mood disorder have been inconclusive about the specific susceptibility genes [19]. Therefore, prenatal depression may not only be caused by one single factor but the interplay between different factors such as genetics and environment [1]. Environmental factors, such as viral infections, hormonal disorders, chronic disease, nutrition deficiency and also social factors, may increase the risk of prenatal depression development in vulnerable individuals who carry specific susceptible genes [20].

The most common treatment for prenatal depression is anti-depressants, for example, selective serotonin reuptake inhibitor (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). A cohort study by Huybrechts et al. showed that 8.1 % of women are exposed to the anti-depressant medications during their pregnancy in the United States from 2000 until 2007 [21]. Although the early report showed that SSRI medications are considered safe during pregnancy in recommended dosage [22], recent studies showed that continuous SSRI exposure may associate with lower gestational age [23], increased risk of pre-term birth [24] and may impact health and behavioural development of the offsprings [25][26]. Therefore, it is urgent to explore other interventions to treat prenatal depression without any adverse effect on the fetus development and neonatal health outcome.

The role of essential fatty acids during pregnancy

Nutrition intake is crucial during pregnancy for both the fetus and mother. A number of studies mentioned that nutrition intake of a mother during pregnancy have impacts toward the children birth outcomes such as low birth weight and preterm birth, which could then increase the risk for the development of some diseases later in life [27]. One of the nutrients that play a critical role during pregnancy is essential fatty acids. Essential fatty acids are polyunsaturated fatty acids (PUFA) that are important for our body and are called essential because the human body cannot synthesize them. Therefore, humans rely on dietary sources to obtain essential fatty acids. These polyunsaturated fatty acids are vital for the new tissues formation as they are the building blocks of the cell membrane [28]. Deficiency in essential fatty acids could lead to dermatitis, alopecia, thrombocytopenia and even intellectual disability in children [29].

Essential fatty acids can be categorized into 2 groups which are linoleic acid (omega-6 or n-6) and alpha-linolenic acid (omega-3 or n-3). Omega-6 can be metabolized into arachidonic acid (AA) while omega-3 fatty acid is metabolized into eicosapentaenoic acid (EPA) and decosahexonic acid (DHA) as depicted in figure 1. Both omega-3 and omega-6 fatty acids are substrates for eicosanoids, the cell signalling molecules which responsible for the regulation of inflammation and immune response. However, in general, omega-6 is the substrates for pro-inflammatory and immune sensitive eicosanoids production while intake of omega-3 makes anti-inflammatory and immunosuppressive eicosanoids [30],[31]. Omega-6 fatty acids are abundant in typical Western diet such as grain-fed beef, processed foods and also liquid vegetable oils whereas omega-3 fatty acids can only be found in a few foods such as oily fish, flax seeds and canola oil [32].

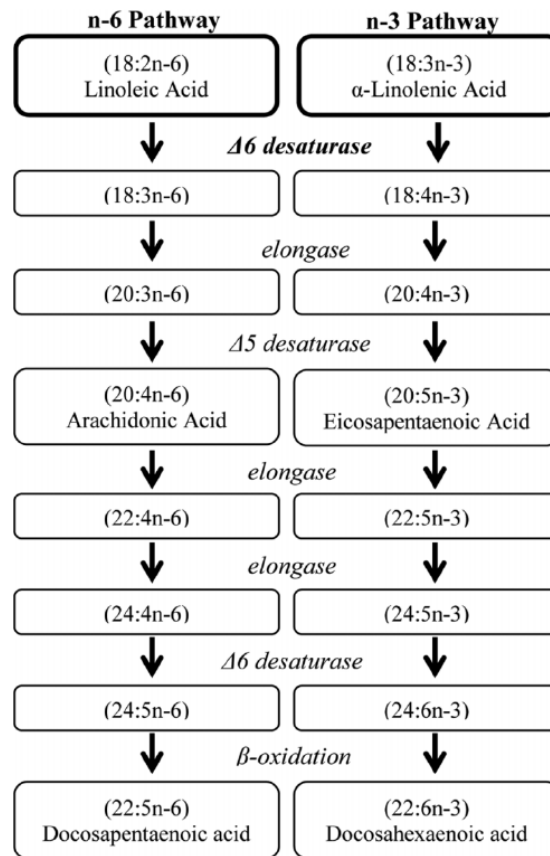


Figure1. Polyunsaturated fatty acids metabolism pathway in mammals [33]

It has been widely acknowledged that essential fatty acids intake is highly associated with healthy pregnancy. This association was initiated by epidemiological findings that showed longer gestation period and higher baby weight in areas that have higher consumption of fish, such as in Faroe Island and Inuit population in Canada, compared with the other community that consume less fish [34],[35]. Another study also displayed that supplementation of fish oil from the 30th week of pregnancy increased gestation period by 4 days and showed a higher mean birth weight compared to control group [36]. A randomized controlled study was conducted in 291 pregnant women in the United States from 24 to 28 weeks gestations to assess the effects of ingestion omega-3 fatty acids on the duration of gestation and birth weight. The results of the study indicated that the gestation period was increased by 6 days in groups who ingest higher DHA. However, they didn't find any significant effects in regards to birth weight [37]. Based on these studies, essential fatty acids consumption indeed seem to have positive results based on gestation period and also birth weight.

Asides from the gestational period and baby weight, maternal essential fatty acids intake is also crucial for the neonatal outcome and development, especially omega-3 fatty acids. The derivative of omega-3 fatty acids, DHA, is found to be vital in the development of fetus brain and retina. An animal study done in rhesus monkeys showed that depletion of omega-3 fatty acids

during prenatal and postnatal development reduced the visual acuity of the infants [38] which suggests the dependence of normal visual function on the intake of omega-3 fatty acids. Also, maternal consumption of omega-3 fatty acids during pregnancy has impacts on behaviour and cognition of the offsprings. An observational cohort study done in 11875 pregnant women showed that low intake of seafood during pregnancy, less than 340 g/ week, was associated with increased risk of lower IQ and also suboptimum outcomes for motor and pro-social behaviour of children compared children of women who had more than 340 gram seafood intake in per week during their pregnancy [39]. Another study displayed that supplementation of DHA for the last 2 trimesters of pregnancy positively affects infants' attention across the first year [40].

Studies also found the relationship between omega-3 fatty acids and preeclampsia incidents. Preeclampsia is a pregnancy complication that impacts 3-5% of pregnancies and is characterized with increased blood pressure and proteinuria together with maternal organ dysfunction such as liver and kidney [41]. This complication is found to be highly associated with essential fatty acids as women with preeclampsia were found to have lower serum levels of omega-3 fatty acids and higher levels of omega-6 fatty acids than women who did not develop preeclampsia [42]. Similarly, one study also displayed that woman with the lowest level of erythrocyte omega-3 fatty acids were 7.6 times more prone to develop preeclampsia compared to women with the highest level of omega-3 fatty acids [43]. The population studies have been conducted to assess the effects of routine supplementation of fish oil on preventing preeclampsia; however no effects of supplementation were found on decreasing the risk of preeclampsia [44].

The ratio of maternal intake of omega-6 to omega-3 fatty acids was also found to be essential during pregnancy and particularly associated with the infant neurodevelopment. An animal study by Sakayori et al, in 2016 showed that feeding pregnant mice with imbalance diet of essential fatty acids, excessive omega-6 and omega-3 deficient diet, impaired neocortical neurogenesis of the offsprings. Furthermore, the offsprings exhibited increasing anxiety-related behaviour in adulthood although they were raised with well-balanced fatty acids diets [45]. A cohort study by Kim et al, in 2017 also found a negative correlation between maternal intake omega-6/omega-3 fatty acids with infant neurodevelopment at 6 months' age. The infant neurodevelopment were assessed with Korean version of the BSID-II (a standardised tool to assess toddler and infant neurodevelopment) [46]. They concluded the study with a suggestion to maintain low ratio of omega-6 to omega-3 during pregnancy.

To sum everything up, maternal intake of omega-3 fatty acids plays a significant role in healthy pregnancy and the ratio of maternal intake of omega-6 and omega-3 is also found to be crucial for infant's neurodevelopment. Various studies have mentioned the beneficial effects of dietary intake of omega-3 during pregnancy in gestational length, birth weight, and neonatal development. Preeclampsia incidents have also been related to low levels of omega-3 fatty acids in pregnant women although studies haven't found any effects on the routine use of marine oil in preventing preeclampsia. Nevertheless, it is vital for pregnant women to obtain adequate omega-3 fatty acids from dietary intake and also try to maintain low ratio of intake of omega-6 and omega-3. Several expert groups, such as the European Commission and the

International Society for the Study of Fatty Acids and Lipids, have recommended women to consume omega-3 fatty acids between 200-300 mg per day during pregnancy and lactation [30].

The association between essential fatty acids and prenatal depression

The essential fatty acid is an important nutrient for the human body, and its consumption is required for sustaining individuals' health, particularly mental health. Recently, essential fatty acids have been gaining attention regarding its relationship with major depressive disorder. A study by Joseph Hibbeln displayed a significant negative correlation between worldwide fish intake and depression prevalence [47]. Also, a cross-sectional survey in New Zealand demonstrated a significant relationship between fish consumption and higher self-reported mental health status [48]. These epidemiological data provide evidence that essential fatty acids, especially omega-3 fatty acids, may indeed play a role in depression.

Women are more susceptible to depression compared to men with global annual prevalence was 5.1% for women and 3.6% for man in 2015 [49]. During pregnancy, women are even at higher risk for depression due to hormonal changes, stress and also changes in life roles. Interestingly, the overall maternal essential fatty acids are declined during pregnancy [50] because maternal-3 omega fatty acids are transported to the fetus via placental transport [51]. One case-control study showed an association between omega-3 fatty acids deficiency and perinatal depression. This study found that women with lower omega-3 fatty acids blood level are 6 times more prone to prenatal depression compare to women with higher omega-3 fatty acids blood level [52]. Associations between prenatal depression and omega 3-fatty acids derivatives were also found in Japan. Prenatal depressive symptoms were significantly associated with lower blood plasma DHA concentration [53]. Taken these studies into account, low level of omega-3 fatty acids may have a role in depressive symptoms during pregnancy. The low level of omega-3 fatty acids corresponds to the inadequate maternal dietary intake of omega-3 fatty acids as a study showed that plasma and erythrocyte concentration of omega-3 derivatives, such as DHA, are positively correlated with DHA dietary intake [54].

To sum it up, insufficient maternal dietary intake of omega-3 fatty acids may be related to prenatal depression. An epidemiological study in Japan has been conducted to assess the relationship between maternal intake of fish and omega-3 fatty acids and prevalence of prenatal depression. They found that indeed higher intake level of fish, EPA and DHA were independently associated with lower depressive symptoms during pregnancy [55]. A similar result was also found by Golding et al., in 2009 who showed that lower maternal intake of omega-3 was related to higher levels of depressive symptoms at 32 weeks gestations. Because of these findings, omega 3-fatty acids supplementation has been studied for its effects on treating prenatal depression and preventing post-partum depression.

Possible mechanisms of the essential fatty acids in depression

Essential fatty acids specifically omega-3 fatty acids have been studied extensively for its therapeutic value on depression; however the underlying mechanisms are still unclear. Several hypotheses have been proposed in regards to the protective role of omega-3 fatty acids. The first mechanism proposed is related to the ability of omega-3 fatty acids to influence the

interaction with the serotonergic and dopaminergic transmission. The pathophysiology of depression is often linked to the monoamine hypothesis which postulates that the symptoms of depression are due to the deficiency in brain monoaminergic transmitter such as norepinephrine, serotonin, and dopamine [56]. Numerous studies showed that altering intake of omega-3 fatty acids could impact the number and function of serotonin (5-HT) and dopamine receptors. Animal studies done by Vines et al in 2012 reported that fish oil supplementation increased serotonin contents in the hippocampus [57] and on the other hand, omega-3 deficiency increased the serotonin receptor (5HT₂) density in the frontal cortex [58]. Similarly, omega-3 deficiency in rats also led to decrease expression of dopamine receptor (D₂R) in the frontal cortex [58] while supplementation of fish oil resulted in 40% increase of dopamine level in the frontal cortex of rats compared to control diet [59].

The derivative of omega-3 fatty acids, DHA, could also modulate the neurotransmitter receptors function through cell membrane fluidity [60]. DHA is the most common fatty acid in the brain which take up nearly 30% of fatty acids content, and its composition in lipid membrane increased cell membrane fluidity [61][62]. The binding of serotonin to its receptor depends on cell membrane fluidity as the cell membrane's fluidity decreased, the ability of serotonin to bind to the receptor significantly reduced because of the low accessibility of the receptors [63][64]. This effect is also applied to other neurotransmitters such as dopamine. Therefore, it is apparent that the omega-3 fatty acids have relation with monoaminergic transmission system which may explain the role of omega-3 fatty acids and its derivatives on depression treatment.

Another possible mechanism is related to the anti-inflammatory effects of omega-3 fatty acids. Recent studies have suggested that immune systems are altered in depressed people and Vogelzangs et al. in 2012 confirmed that there was an elevated inflammation in blood sample of depressed men, particularly in late-onset depression [65]. Animal studies also showed that injecting lipopolysaccharides, a bacterial endotoxin cells usually used for inducing inflammation, leads to depressive behaviour in the tail suspension and forced swimming test [66];[67]. Tail suspension and forced swimming test are experimental methods used to measure stress levels in rodents and usually performed to screen the potential or measure the efficacy of anti-depressant drugs [68];[69]. Pro-inflammatory cytokines, such as IL-1, IL-12, IL-6, and TNF- α , have also been found increased in serum of depressed patient [70]. In contrast, anti-inflammatory manipulations such as knocking out pro-inflammatory cytokines like IL-6 and IL-1 proved to reduce depressive-like behaviour in several behavioural tests in the animal [71]. Omega-3 fatty acids have been reported to play a role in modulating pro-inflammatory cytokines production which may be beneficial in treating depression. It is well-documented that omega-3 fatty acids can dampen inflammation through several pathways including inhibiting of pro-inflammatory eicosanoids formations and also by forming several anti-inflammatory lipid mediators. These pathways contributed in suppressing the activity of NF- κ B, nuclear transcription factor, and reduce the production of pro-inflammatory cytokines such as TNF- α and IL-1 β [72].

The effects of omega-3 fatty acids supplementation on prenatal depression treatment and prevention of post-partum depression

Intervention studies have been done in these past few years to assess the efficacy of omega-3 fatty acids supplementation as a treatment for prenatal depression and to prevent post-partum depression. A randomized, double-blind and placebo-controlled trial was conducted in Taiwan for 8 weeks to examine the efficacy of omega-3 mono-therapy for prenatal depression. The participants were 18-40 year olds pregnant women, with major depressive disorder onset between 16th - 32nd weeks of gestations. Participants were firstly screened with Taiwanese version of the Edinburgh Postnatal Depression Scale (EPDS) and Mini-International Neuropsychiatric Interview. Subjects then received either omega 3 fatty acids with 2.2 g of EPA and 1.2 g of DHA or placebo (olive oil ethyl esters) per day. In total 24 subjects completed the trial. The treatment efficacy of depression was assessed with Hamilton Rating Scale for Depression (HAM-D) as primary measurement while EPDS and Beck Depression Inventory (BDI) were used as secondary measurement. The assessments were taken at weeks 2, 4, 6 and 8. EPDS, HAM-D, and BDI are validated scales to measure the severity of depression where higher value or scores correlate to severe depression. At week 6 and 8, subjects in omega-3 groups had significantly lower HAM-D scores compared to placebo group and also higher response rate and remission rate at weeks 4, 6 and 8. The study also records lower depressive symptom ratings on the EPDS and BDI scores in omega-3 fatty acids group compared to placebo group at week 8. This study suggested that omega-3 fatty acids may have therapeutic value in prenatal depression[73].

The beneficial impact of omega-3 fatty acids on prenatal depression is also displayed by one clinical trial in 2014 [74]. The double-blind clinical controlled trial was done on 80 women who suffered from mild depression. The participants were primiparous (pregnant for the first time) women over 20-week gestations, obtaining 14-19 scores in BDI which indicated a mild depression, and were above 18 years old. During a 6 weeks trial, the participants randomly received either omega-3 (1 g/day) or placebo groups (olive oil), and the depression score was assessed using BDI at week 1 and 6. By the end of the study, the mean of depression scores before and after interventions decreased significantly in both groups where omega-3 groups have higher mean difference (mean difference: 7.35 ± 6.18) compared to placebo groups (mean difference: 2.7 ± 7.2). Based on their outcome, they concluded that omega-3 supplementation might provide a suitable method for mild depression in pregnant women.

In contrast, a number of studies did not find any therapeutic effect of omega-3 fatty acids on prenatal depression treatment and post-partum depression prevention. A double-blind, randomized controlled trial was conducted to test the effects of EPA and DHA fish oils supplementation on preventing depression among pregnant women. The study included 126 pregnant women at risk for depression (EPDS score 9-19, in a scale 1-20) and gestational period of 12-20 weeks. Participants were randomly assigned to receive EPA rich fish oil, DHA rich fish oil or soy oil as placebo. The efficacy of the supplementation was tested by BDI at 26-28 weeks, 34-36 weeks and 6-8 weeks post-partum. By the end of the study, 118 women completed the trial, and they have found no differences in BDI scores between groups at 3-time points after supplementation compared to baseline. Although no difference of BDI scores between groups, they mentioned that serum-DHA concentrations were inversely proportional to

BDI scores in late pregnancy. To sum it up, they concluded that omega-3 supplementation, either EPA or DHA, didn't prevent prenatal and post-partum depression [75].

Other studies also have failed to show the therapeutic effects of omega-3 fatty acids on depression during pregnancy and post-partum pregnancy. Rees et al. in 2008 published results in a double-blind randomized placebo-controlled trial on the effect of omega-3 fatty acids treatment in prenatal and post-partum depression. A total of 26 subjects were enrolled in the study with inclusion criteria such as women in their third trimester of pregnancy to 6 months postnatal and also older than 21 years old. Subjects were also screened with EPDS and required to score at least 13 and either >14 on the 17-item Hamilton Depression Rating Scale (HAM-D) or >25 on the Montgomery Asberg Depression Rating Scale (MADRS). The interpretation of EPDS, HAM-D and MADRS results are mentioned in Appendix. The trial was conducted for 6 weeks and the participants either received placebo or 6 gram fish oil per day. The depression score was measured from baseline to week 6. After 6 weeks of supplementation, they found that mean depression scores (across 3 measurement) from baseline to week 6 were significantly decreased in both groups which indicated a significant improvement however they found no statistically significant differences in the mean of depression scores between the treatment and placebo group. Therefore, they suggest that omega fatty acids supplementation does not have any benefit over placebo in treating prenatal and post-partum depression [52].

Intervention studies were also conducted in healthy pregnant women with low frequency of fish intake to see whether supplementation of low doses DHA or DHA and AA could prevent any depressive symptoms during pregnancy and lactation [76]. One hundred nineteen pregnant women completed the study, and they are daily supplemented with placebo, DHA only (220 mg) or DHA+AA from (220 mg each) week 16 during pregnancy until three months post-partum. The depression scores were assessed at 16, 36 weeks of pregnancy and 6 weeks post-partum using EPDS. Results revealed that supplementation of low dosage DHA or DHA+AA did not affect mean of EPDS scores, incidence or severity of post-partum depression in a population based sample with low frequency of fish intake.

Author, year [reference]	Design and sample size (n)	Measurement	Outcomes	Conclusion
Su et al., 2008 [73]	8 weeks randomized, double blind, placebo controlled trial with n-3 PUFAs (n=13) and placebo (n=11) in pregnant women with major depressive disorder (DSM-IV criteria)	Screened used : Taiwanese version of the EPDS and MINI. HAM-D used as primary measures while; EPDS and BDI for secondary measurement at week 0 (baseline), 2,4,6 and 8.	Subjects in group omega-3 had lower mean HAM-D scores at week 6 (p=0.001) and 8 (p=0.019) compared to placebo. The EPDS and BDI scores were also lower on omega-3 fatty acids compared to placebo at week 8	Omega-3 fatty acids may have therapeutic value in prenatal depression.
Kaviani et al., 2014 [74]	6 weeks double blind randomized controlled clinical trial, n=80 primiparous women suffering from mild depression obtained either omega-3 fatty acids (dosage :1g/day, n=40) or placebo (olive oil, n=40)	BDI scores before and after intervention (at week 6).	Lower depression scores were recorded in both group after treatment where omega-3 group have p value <0.001 while control has p value<0.021. Omega-3 group has higher mean difference (7.35±6.18) compared to control (2.7±7.2)	Omega-3 supplement may be a suitable treatment for mild depression during pregnancy for short period of time
Mozurkewich et al., 2008 [75]	A double-blind, randomized controlled trial with 118 subjects completed the trial. The subjects were randomly assigned with either EPA-rich fish oil (1060 mg EPA +274 mg DHA, n=39), DHA rich fish oil (900 mg DHA+180 mg EPA, n=38) or soy-oil as placebo (n=41).	Screened used: EPDS (EPDS scores: 9-19) and MINI. BDI was administered at at 12-20 weeks', 26-28 weeks', 34-36 weeks' gestations and 6-8 weeks' post-partum. Serum fatty acids were analysed at baseline and at 34-36 week pregnancy.	No differences in the mean of BDI scores between groups at baseline compared to any point of time. Supplementation of omega-3 fatty acids increasing serum EPA in EPA group and DHA in DHA group significantly.	Both treatment with EPA and DHA supplementation did not prevent depressive symptoms during or after pregnancy
Rees et al., 2008 [52]	Total 26 subjects (from third trimester pregnancy to 6 months postnatal) were participated in a 6 weeks randomized double-blind placebo trial. Subjects were either received 6g/day fish oil (n=13) or placebo (n=13).	Screened used: EPDS (score >=13) and either >14 on HAM-D (scale 17) or >25 on MADRS. The outcomes measurement are EPDS, HAM-D and MADRS scores from baseline until week 6 (the scores were assessed weekly)	Mean changed depression score from baseline to the week 6 in both groups showed significant improvement (p<0.001) however no statistically significant difference in the fish oil group compared to placebo group.	No beneficial effect of omega-3 fatty acids treatment over placebo in treating prenatal and post-partum depression.
Doornbos et al., 2009 [76]	119 women completed the trial and supplemented daily with placebo (n=36), DHA (220 mg, n=42) or DHA+AA (220 mg each, n=41).	Depressive symptoms were measured with EPDS at week 16, 36 pregnancy and 6 weeks post-partum.	No significant difference of EPDS scores between week 36 of pregnancy and 6 weeks post-partum in any group.	Low supplementation of DHA or DHA+AA does not prevent prenatal and post-partum depression in healthy pregnant women with low fish intake

EPDS = Edinburgh Postpartum Depression Scale, BDI = Beck Depression Inventory, HAM-D= Hamilton Rating Scale for Depression, MADRS= Montgomery Asberg Depression Rating Scale, PUFA = polyunsaturated fatty acids, EPA= eicosapentaenoic acid, DHA = docosahexonic acid, AA = arachidonic acid.

Table1. Summary of omega-3 fatty acids intervention studies in treatment of prenatal depression and prevention of post-partum depression.

Future prospective

The previously mentioned studies have shown mixed results regarding the effects of essential fatty acids, especially omega-3 fatty acids, supplementation to prenatal depression treatment and post-partum depression prevention. Two randomized controlled trial [73],[74] suggested beneficial effects of omega-3 fatty acids on prenatal depression treatment whereas three other supplementation studies [75],[76],[52] did not show any therapeutic value of omega-3 fatty acids on depression. The heterogeneity of the studies design may contribute to the different outcome produced, for instance, different dosages, length of the trials and starting point of supplementation, which then lead to difficulties in interpreting the results. Additionally, several studies [75],[76],[52] did not focus only on prenatal depression treatment but also on post-partum depression which makes it difficult to examine the effects of omega-3 fatty acids solely on prenatal depression treatment. Therefore, further studies need to be conducted to examine the effects of essential fatty acids supplementation strictly on prenatal depression treatment. Larger samples sizes are recommended for future studies as previous studies were conducted on very small sample sizes. Also, a higher dosage (>2 gram of fatty acids) may also show more beneficial effects [73] compared to low dosage as previous supplementation studies [76] with

small dosages (220 mg omega-3 fatty acids/ day) did not show beneficial effects on prevention of post-partum the depression.

Conclusion

To sum everything up, prenatal depression is one form of depression that occurs during pregnancy and may negatively affect mother and the development of the offspring. The majority of the cases are still undertreated and underdiagnosed. The treatment of the prenatal depression itself is still exposed to problems as the most common treatment for depression, SSRIs, may affect fetus' health. Therefore, there is a need to explore other interventions that may not impact, or only beneficiary, the developmental of the fetus. Essential fatty acids, especially omega-3 fatty acids, supplementation is proven to be crucial for a healthy pregnancy, and its deficiency has been linked to prenatal depression. Intervention studies have been done to assess the efficacy of omega-3 fatty acids supplementation on treating prenatal depression; however, published studies have showed mixed results. Based on previous studies, the role of essential fatty acids supplementation on prenatal depression treatment remains inconclusive. However, this specific nutrient might be a promising therapeutic tool for depression as omega-3 fatty acids have a particular role in monoaminergic transmission and are also considered safe during pregnancy. Thus, future trials need to be conducted to establish the role of essential fatty acids solely on prenatal depression treatment. Larger sample size and also higher dosage of supplementation might be points of considerations for future trials.

Appendix

Interpreting EPDS, HAM-D, MADRS and BDI scores

EPDS results

Total score of 13 or greater are generally indicating that the woman is highly to be depressed (cut-off score 13)[77].

BDI results

The scale is 0-63 where score 0-13 considered as minimal range, 14-19 as mild depression, 20-28 as moderate depression and 29-63 as severe depression [78].

17-item HAM-D results

0-7 is normal, 8-16 is mild depression, 17-23 is moderate depression, and over 24 is severe depression with 52 as maximum score [79].

MADRS

The cut-off scores are 0-6 is normal, 7-19 considered as mild depression, 20-34 is moderate depression and more than 34 is severe depression [80][81].

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