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RESEARCH

Review

Perinatal Depression: Prevalence, Risks, and the Nutrition Link—A Review of the Literature

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ABSTRACT

The purpose of this review is to examine the role of nutrition in perinatal depression. Perinatal (maternal) depression refers to major and minor episodes during pregnancy (termed *antenatal*) and/or within the first 12 months after delivery (termed *postpartum* or *postnatal*). Prevalence of antenatal depression can be as high as 20%, while approximately 12% to 16% of women experience postpartum depression. These are probably conservative estimates, as cases of maternal depression are underreported or underdiagnosed. Risk factors for depression include genetic predisposition and environmental factors, as well as a number of social, psychological, and biological factors. One biological factor given increasing consideration is inadequate nutrition. Credible links between nutrient deficiency and mood have been reported for folate, vitamin B-12, calcium, iron, selenium, zinc, and n-3 fatty acids. For maternal depression, the nutrient that has received the most attention from nutrition researchers has been the n-3 essential fatty acids. Numerous studies, such as randomized controlled trials, cohort studies, and ecological studies, have found a positive association between low n-3 levels and a higher incidence of maternal depression. In addition, nutrient inadequacies in pregnant women who consume a typical western diet might be much more common than researchers and clinicians realize. A number of studies have reported inadequate intakes of n-3, folate, B vitamins, iron, and calcium in pregnant women. Depletion of nutrient reserves throughout pregnancy can increase a woman's risk for maternal depression.

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There is growing concern about the rising prevalence of mental illness in the world (1). One of the major mental health problems has been mood disorders, the most common of which, worldwide, is depression. According to the World Health Organization (WHO), depression was the leading cause of disability worldwide and the fourth leading contributor to the global burden of disease (the disability adjusted lives per years) (2). By the year 2020, WHO predicts that depression will be the second largest contributor to the global disability adjusted lives per years for all ages and both sexes (2). Today, depression is already the second largest cause of disability adjusted lives per years for those of reproductive age (15 to 44 years of age). Women are two to three times more likely to experience depression than men (3). The consequences of depression in women impart greater importance during or after pregnancy. While depression in general can have devastating effects on families and the community, maternal depression has much more serious and long-lasting consequences for the children in the family, as we will show here.

There are a number of theories about the causes and risk factors for depression. This article will examine the link between food and mood, one possible cause of depression that is of growing interest in the scientific community (4-7). Findings presented in this article will demonstrate that diets with various nutrient deficits are more common than recognized (8,9), and that such deficits can contribute to maternal depression.

The purpose of this review is to examine the prevalence of depression in women during pregnancy and the postpartum period, and then to assess whether nutrition might play a role. The literature on the relationship between food and mood raises the question of whether nutrient deficiency might be a substantial contributor to development of depression in women during and after pregnancy.

PERINATAL DEPRESSION

Perinatal depression refers to major and minor episodes during pregnancy (termed *antenatal*) or within the first 12 months after delivery (termed *postpartum* or *postnatal*) (10). The term *maternal depression* has also been used interchangeably with perinatal depression. Signs and symptoms for perinatal depression are the same as those for depression in the general population: depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration (11).

To date, there are no diagnostic criteria for perinatal depression per se; diagnosis is based on the *Diagnostic and Statistical Manual*, 4th edition, or the *International*

Statistical Classification of Diseases, 10th edition (11). Prevalence of antenatal depression appears to peak in the first trimester, while postpartum depression peaks around 12 weeks postdelivery (10). Both scientific research and public awareness have focused primarily on postpartum depression; however, it is now recognized that antenatal depression is just as problematic (perhaps more) as postpartum depression, and the two might be a continuum reflecting an underlying chronic condition among women during pregnancy and thereafter.

ANTENATAL DEPRESSION

Antenatal depression is a major health problem, but is less well-studied than postpartum depression (11). It has been estimated that prevalence of antenatal depression might be as high as 20% (12). For example, a cross-sectional study of 432 women seen in a private Brazilian clinic used the Beck Depression Inventory as a screening tool and reported a prevalence of 19.6% for antenatal depression (13). Previously, in a larger sample of >3,000 pregnant women in the United States, 20% scored above the cutoff for depression on the Center for Epidemiological Studies Depression Scale (14). Both measures used in these studies are well-validated for self-report of mood and the similarity of prevalence rates is striking. A systematic review by Bennett and colleagues found prevalence rates at 7.4%, 12.8%, and 12.0% for first, second, and third trimesters, respectively (15). These are likely to be conservative estimates, as women who are depressed are less likely to participate in research studies.

POSTPARTUM DEPRESSION

Postpartum depression (PPD) has received more attention in the medical and scientific literature than antenatal depression. Published estimates indicate that approximately 12% to 16% of women experience PPD (16). Like antenatal depression, this is probably a conservative estimate, as cases of PPD are underreported or underdiagnosed. In fact, a review by Gavin and colleagues estimated that as many as 19% of new mothers might suffer from depression within the first 3 months after giving birth (10). PPD emerges most often within 6 to 12 weeks of delivery, but can occur any time up to 1 year after birth (16). Longitudinal studies have found that depression in the postpartum period can last for months or even years after giving birth (17,18).

EFFECTS OF MATERNAL DEPRESSION

Maternal depression is a serious mental health problem that can negatively affect the lives of women, children, and their families (4,19,20). The impact of PPD and antenatal depression must be considered in terms of both the women's own lives and their children's. Deleterious effects of maternal depression on a child's functioning in cognitive, social, and developmental areas are well-documented in the literature (20-22). For the woman, depression during pregnancy has been linked to poor maternal self-care and outcomes (15). Depressed pregnant women are less likely to seek proper medical care during pregnancy and more likely to engage in risk-taking activities, such as alcohol or drug abuse (12). Poor obstetric outcomes in women with antenatal depression include preeclampsia, birth difficulties for the mother and child, and almost seven times the risk for postpartum depression (23). Maternal depression has also been associated with increased risk of preterm delivery and reduced breastfeeding (12).

For the newborn, maternal depression is strongly associated with lower APGAR (American Pediatric Gross Assessment Record) scores, failure to thrive, and poor physical and emotional/behavior development (24,25). A study of 9,244 families in the southwest of England reported developmental delays in babies aged 18 months whose mothers were depressed (26). Another study found maternal depression was associated with poorer growth (underweight and stunting) and greater risk of diarrheal disease in a sample of infants in Pakistan (27). A review of cross-sectional and cohort studies by Stewart reported that maternal depression was associated with poor infant physical growth, infant malnutrition, and increased problems such as respiratory and diarrheal illness (24). Furthermore, children of depressed women are also at greater risk for lower scores on developmental scales, exhibit reduced motor tone and activity, and have more behavioral problems (28), such as sleep disturbances and irritability (12). Even more disturbing was a study that found that the offspring at 16 years were almost five times more at risk for depression when born to women with antenatal depression, compared with adolescents born to women without antenatal depression (29). The role of genetic predisposition may be an influence in such data. Thus, maternal depression has broad implications for maternal and child mental and physical health that may have long-lasting social and economic impact (30,31).

It is important to consider that causal arrows may point in both directions: maternal depression can influence child development, but poor infant outcomes can also affect maternal mood. In the case of PPD, it is possible that infant illness, such as failure to thrive for medical reasons or congenital diseases, can contribute to depression in new mothers (see Figure 1). A newborn with an illness is a considerable additional stressor for a family that is already challenged by the adaptations to changes in their routine and meeting the needs of the baby. However, this bidirectional causal pathway does not explain the fact that the incidence of poor birth outcomes is low relative to the incidence of postnatal depression. In other words, mothers experience postnatal depression at a much higher rate than the number of babies born with poor birth outcomes. Thus, risk factors other than poor infant outcome are likely to play a larger role in maternal depression.

RISK FACTORS FOR MATERNAL DEPRESSION

Symptoms of general depression are variable among patients and, consequently, depression has been viewed not as a single disease, but as a syndrome encompassing a spectrum of mood symptoms with multiple causes and possibly multiple pathophysiologies (32). These multifactorial causes of depression likely involve both genetic and environmental factors (33). The genetic basis of mood disorders has been studied extensively. Craddock and Forty reviewed linkage, genetic, family, and twin studies and found evidence implicating specific genes with regard to depression and schizophrenia (33). However, replica-

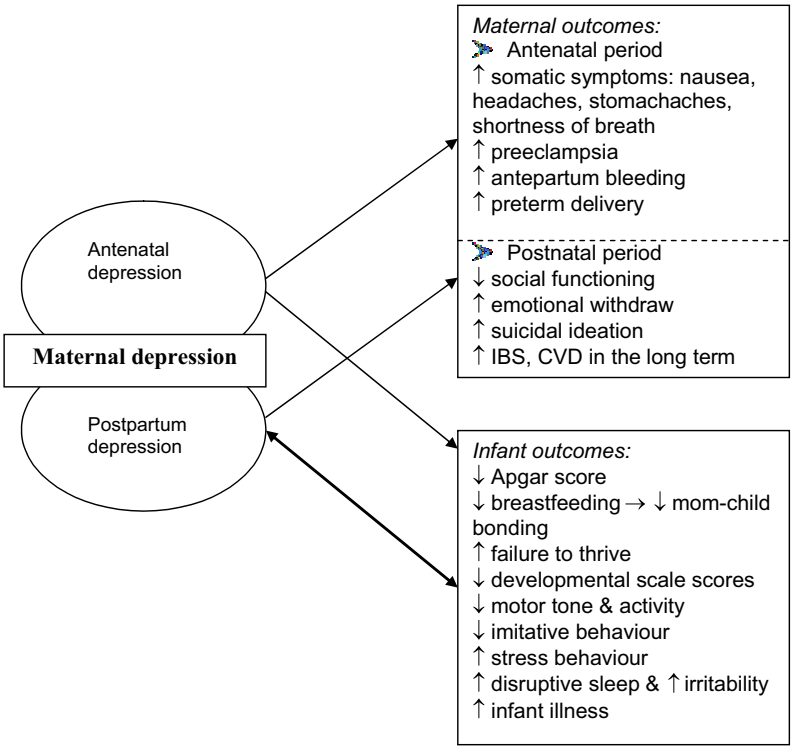

Figure 1. Schematic model illustrating the effects of maternal depression on maternal and infant outcomes (12). APGAR=named after Dr Virginia Apgar for assessing Appearance, Pulse, Grimace, Activity, Respiration in newborns. CVD=cardiovascular disease. IBS=irritable bowel syndrome.

tion of these studies is needed, in addition to studies on phenotypic relationships and biological mechanisms, to determine degree of genetic causality.

Degree of interplay among the different factors is unclear. For example, epidemiological data have shown about 40% to 50% of the risk for depression is linked to genetics (32), but genetic studies on mood disorders have yet to provide conclusive evidence of specific susceptibility genes or their pattern of inheritance (34). Uncertainties are likely a result of the complex nature of the disorder and the involvement of multiple genes and gene interactions. Thus, it is likely that genetic predisposition, in combination with an array of environmental influences, is involved in development of depression.

Environmental factors associated with depression include stress (eg, physical, mental, and emotional trauma); viral infections; hormonal disorders; chronic diseases (32); drugs such as oral contraceptives; and some medications (eg, sedatives) (35). However, environmental factors do not act alone; they can increase the risk for depression in those with a genetic susceptibility for the disease.

In addition to genetic predisposition and environmental factors that influence the incidence of depression, a number of social, psychological, and biological factors have been associated with risk for maternal depression in particular. Social risk factors include lack of partner or marital difficulties (eg, divorce) (36), low socioeconomic status (eg, financial insecurity/hardship) (37,38), poverty, lack of social support (13,39,40) or social isolation (41), major life events (42), family violence (eg, history of abuse) (42), increased life stress, and substance abuse (12). Psychological factors include current depression or anxiety (43), history of depression (38,43), and history of psychiatric illness (41), such as premenstrual dysphoric disorder and mood symptoms during the third trimester (44). Research into social and psychological factors associated with maternal depression has been extensive.

The set of biological risk factors associated with maternal depression is more difficult to ascertain. Biological factors that contribute to the pathophysiology of maternal depression include hormonal influences (28,45), neurotransmitter function (46-48), and nutrient deficiencies because of malnutrition or poor diet quality (4).

PATHOPHYSIOLOGY OF MATERNAL DEPRESSION

A number of mechanisms have been proposed for the pathophysiology of maternal depression, including the hypothalamic-pituitary-adrenal (HPA) axis and the role of cortisol (49,50). Findings from studies on cortisol and the HPA axis have been contradictory. For example, Jolley and colleagues reported that there was no relationship between adrenocorticotropic hormone and cortisol levels in subjects with PPD (50). In contrast, the normal reaction of higher adrenocorticotropic hormone and lower cortisol levels was demonstrated in a control group, suggesting that there was some form of "dysregulation" of the HPA in those with PPD (50). However, Zonana and Gorman reviewed a number of studies that showed no association between cortisol levels and PPD (49).

Hormones are another mechanism hypothesized to be

involved in the pathophysiology of maternal depression; they include progesterone, estradiol and estriol, prolactin, thyroid-stimulating hormone, and triiodothyronine/thyroxine (49,51-53). It is well-known that hormonal levels change drastically during and after pregnancy. For example, estradiol levels increase 50 times and progesterone levels 10 times by the third trimester, and they normalize within 1 to 2 weeks postpartum. However, no association has been found between the changes in hormonal levels and the peak incidence of depression during or after pregnancy (49). Elevated thyroid-stimulating hormone has been found to be associated with higher depression scores (54). Another study found higher risk for PPD symptoms in women with lower levels of antenatal total and free thyroxine levels (48). A number of other studies have examined the role of hormones on PPD; a detailed review is available elsewhere (49). In summary, however, the role of specific hormones remains uncertain.

A majority of the research on the pathophysiology of depression has focused on the monoamine neurotransmitters (serotonin, norepinephrine, and dopamine) (46-48). A review by Nemeroff reported decreased or altered levels and activity of the three monoamine systems in the brains of patients with depression (55). Previous research has examined serotonin as the main neurotransmitter responsible for depression. However, in light of the evidence on the lack of efficacy of antidepressants, such as selective serotonin reuptake inhibitors and selective serotonin-norepinephrine reuptake inhibitors, studies into the dopaminergic system (responsible for pleasure) have increased (46,49). In other words, it is unlikely that a single neurotransmitter system is responsible for the symptoms of depression. Although there is likely an association between the monoamine systems and maternal depression, the literature on pregnant or postpartum women is limited.

An element common to the various mechanisms described here is nutrition. Nutrition provides the basic elements required for biochemical pathways to ensure proper physical and mental development and function; ie, nutrients provide the underlying foundation for proper function of the HPA axis, other endocrine systems, and neurotransmitter pathways. The general role of nutrition in depression has recently become a focus of investigations. This evidence is best reviewed in the broader context of the role of nutrient intake in relation to mood.

NUTRITION AND MOOD

Research on the relationship between nutrition and brain function is remarkably large and reaches back almost 90 years (56-58). Credible links between nutrition and mood have been reported for folate (59), vitamin B-12 (4,60), calcium (60,61), iron (4,60,62), selenium (4,63), zinc (4,64,65), and polyunsaturated fatty acids (PUFAs) (4,66-73). A review of correlational and intervention studies by Kaplan and colleagues found potentially beneficial effects of many vitamins (especially B vitamins and vitamins C, D, and E), minerals (calcium, chromium, iron, magnesium, zinc, and selenium), and vitamin-like compounds (choline) on mood symptoms (56).

Individual nutrients have been studied with respect to their role in a number of neural and endocrine pathways, including how their deficiency may contribute to the pathophysiology of depression. One of the well-studied vitamins is folate, which is required for the biosynthesis of the three monoamine neurotransmitters, serotonin, dopamine, and norepinephrine. The active metabolite of folate, 5-methyltetrahydrofolate (5-MTHF, L-methylfolate), is required for remethylation of homocysteine in the production of methionine, which is involved in a number of biochemical processes involving the three aforementioned neurotransmitters (74). Thus, a deficiency in folate would impact the production and function of these neurotransmitters. Another vitamin involved in neurotransmitter pathways is vitamin B-6, which is a cofactor in the production of serotonin from tryptophan. Low plasma levels of the B-6 derivative, pyridoxal phosphate, have been associated with symptoms of depression (75). Vitamin B-12 is another nutrient that is crucial to neurological function. B-12 is a cofactor in the formation of S-adenosylmethionine, an intermediate for production of the neurotransmitters (76). There is evidence from research on laboratory animals that vitamin D, in the form of 1α,25 dihydroxyvitamin D-3, may be involved in anterior pituitary lobe function, as well as in dopamine concentration in the cortex (77). In humans, a study by Lansdowne and Provost found vitamin D to enhance mood in seasonal affective disorder (78). Another nutrient linked to mood is zinc. Studies have reported an association between low zinc status and depression; there is also evidence that intervention with zinc has an antidepressant effect (64,79). It has been suggested that zinc can influence serotonin uptake (79). Researchers are just beginning to examine individual nutrients and their role in biosynthesis, metabolism, and function of various hormones and neurotransmitters. Much more work is needed to understand their roles. The physiological mechanisms of some nutrients and their effects on brain/neurological function are summarized in Figure 2.

NUTRITION AND MATERNAL MOOD

While specific nutrients associated with depression in the general population have been demonstrated, little is known about low nutrient levels and maternal depression. Most studies on specific nutrients (eg, vitamins and minerals) and mood have excluded pregnant women. However, it is known that pregnant women are especially susceptible to the effects of low nutrient intakes (4). During pregnancy and lactation, nutritional requirements are increased so that fetal and infant growth are adequately supported, as well as maternal metabolic needs specific to reproduction (80). In other words, the fetus is preprogrammed with specific energy and nutrient needs in order to grow and develop at set times during gestation, and these needs must be met by the mother. Nutrient demands from the fetus change over time and during different developmental stages (81). Thus, it is important that pregnant women select foods with enhanced nutrient density in order to avoid risking nutritional inadequacy, which may have long-lasting effects on both the women and their children (80). Picciano (80) summarized the increased overall nutrient requirements of pregnant women compared with nonpregnant women; however, the nutrient that has received the most attention in relation

Nutrient	Mechanism of action	Deficiency effects
Vitamin B-1 (thiamine)	Facilitates glucose use for energy production (decarboxylation, transamination, oxidation, reduction reactions) (57)	Neurological changes, including confusion, apathy, decreased short term memory, and irritability (106); in rat models, selective neuronal cell death in thalamic structures (57)
Vitamin B-6	Chemical mediator synthesis; alters N-methyl-D-aspartate receptors in the central nervous system (107)	Asthenia, irritability, depression (57)
Vitamin B-12	Works with folate in methionine-synthase–mediated conversion of homocysteine to methionine, which is essential for nucleotide synthesis and methylation (108)	Neurological disorders, psychotic disturbances, hematological alterations; memory loss, pain, abnormal sensations of extremities (108)
Folic acid	Methionine-homocysteine metabolism (57)	Neural tube defects; megaloblastic anemia with affective (mood) disturbances (84,86)
Vitamin D	Protects neurons of hippocampus, modulates transport of glucose to the brain (109)	Hypothesized role of prenatal hypovitaminosis D on adult neuropsychiatric outcomes (109)
Iodine	Major constituent of thyroid hormones, affects gene expression of other hormones and growth factors (107)	Reduced IQ; cretinism and mental retardation in children born to iodine-deficient moms during pregnancy; hypothyroid-associated depression (107)
Iron	Myelination and lipid metabolism; alters neurotransmission, energy production and DNA synthesis (107)	Reduced learning and memory, behavioral abnormalities (affect and interpersonal interactions) (107); impaired mood and cognition (89)
Selenium	Component of selenoprotein glutathione peroxidase, which plays an important role in the antioxidant mechanisms; required for synthesis and metabolism of thyroid hormones (63)	At times of deficiency the brain retains selenium to a greater extent than any other organ; low selenium intake associated with poorer mood (63)
Zinc	DNA and protein synthesis (107)	Impaired learning and response to stimuli, reduced activity and attention (107); impaired body accumulation of polyunsaturated fatty acids (57)
n-3 fatty acids	Constituent of cell membranes, substrate for lipid-derived mediators for cell-to-cell communication and signal transduction (107)	Impaired vision, hearing, olfactory functions; reduced membrane renewal, thus accelerated cerebral aging; thought to be associated with mood, depression, dementia; may have role in prevention of aforementioned disorders (7)

Figure 2. Mechanism of action and neurologic consequences of deficiency for some nutrients relevant to mood.

to maternal depression has been the n-3 essential fatty acids.

ESSENTIAL FATTY ACIDS AND MATERNAL MOOD

Essential fatty acids are PUFAs, categorized into two main groups: linoleic acid (n-6) and α-linolenic acid (n-3). These fatty acids are termed *essential*, as the body does not produce them and they must be obtained through our diet (82). The two n-3 fatty acids most relevant for brain development and function are eicosapentanoic acid (EPA) and docosahexaenoic acid (DHA), of which the latter is the most prominent in the brain. EPA and DHA can be synthesized in the body from α-linolenic acid. The n-3 fatty acids are essential for receptor function, neurotransmitter uptake, and signal transmission. They are also precursors to specific prostaglandins and leukotrienes (chemicals that dilate blood vessels and prevent clotting) (83,84). The amount of n-3 in the modern diet has declined with the decreased intake of sources of n-3 fatty acids (particularly those coming from marine sources). In addition, there has been an increase in the amount of n-6 fatty acids in the modern diet, which can interfere with the metabolism and synthesis of DHA and EPA (83,85).

Links between n-3s (EPA and/or DHA) and perinatal depression have been examined in a number of observational and intervention studies (see Figure 3), as well as review articles that have reported inconsistencies among the empirical studies. A review by Freeman found inconsistent results in clinical trials with EPA and/or DHA; some results were better than placebo, while others were not (86). Sample size and duration of follow-up were reported to be problematic in some of the study designs. Another review by Hosli and colleagues found mixed results also; findings from a meta-analysis were inconsistent, and clinical studies contradicted observational studies (87). However, a review of epidemiological evidence and intervention studies by Rees and colleagues reported an association between low n-3 intake and depression (67). An analysis of ecological studies from 23 countries by Hibbeln revealed that high DHA levels in breast milk and higher seafood consumption were positively predictive of lower rates of postpartum depression (71). De Vriese and colleagues (68) found that n-3 levels were considerably lower in women who developed PPD than in women who did not. After their critique of study designs and the methodological rigor of multiple case-control

studies, cohort studies and double-blind randomized trials, Sontrop and Campbell concluded that a relationship between n-3 PUFAs and depression was biologically plausible (88).

VITAMINS/MINERALS AND MATERNAL MOOD

Outside the PUFA literature, a thorough search of the peer-reviewed journal databases found limited research on vitamin/mineral deficiency and maternal depression. Beard and colleagues reported a strong relationship between maternal iron status and depression in a study that followed mothers of full-term normal birth weight babies from 10 weeks to 9 months postpartum (89). In another example, results from a study by Wójcik and colleagues showed a relationship between decreased serum zinc concentration and higher scores on the Edinburgh Postpartum Depression Scale (90).

It is recognized that nutrients do not work alone in biochemical pathways that influence mood. A few studies have examined other nutrients in relation to mood disorder in pregnant women, with varying results (61,91). A number of limitations associated with the studies reviewed here (from examining a single nutrient to using a single diet questionnaire) have been recognized. More research into the use of n-3 fatty acids and other nutrients as potential treatment or prophylactic supplements for depression in women in the antenatal and postnatal periods is needed. The limitations in these studies are similar to those of studies that have examined other specific nutrients and mood, and will be reviewed next.

LIMITATIONS OF STUDIES

A review of the literature showed that studies have been both correlational (eg, finding that depressed patients suffer from poor nutrition) and interventional (eg, demonstrating improved mood following supplementation). However, the evidence on how nutrition affects women's mental health during pregnancy or in the postpartum period is limited. The strengths of some of the studies cited here have been in the identification and correlation of specific nutrients with depression. However, with the exception of studies on n-3, most research that examined the interrelationships between nutrition and depression has excluded pregnant or lactating women.

Numerous studies were ecological or cross-sectional, measuring nutrition and depression simultaneously and, consequently, causal relationships cannot be determined. For example, one of the diagnostic criteria for depression is the experience of altered appetite and body weight, which can in itself result in poor nutrition (21). Randomized controlled trials in this area usually consist of short follow-up periods (eg, <12 weeks), small sample sizes, a single nutrient intervention being studied, and homogeneous samples that do not include pregnant women (4). These findings do not reflect real-life practices in which nutrients do not function alone in affecting mood and physiology. Thus, multiple nutrients need to be examined concurrently. Furthermore, a number of studies use a single food frequency questionnaire or a single diet recall as estimates of "average" nutrient intake (92,93). But such point-specific measurements are inadequate in assessing the overall nutrient intake in the sample and might not reflect the nutrient intakes of the population (68,86).

Previous investigations rarely assessed overall nutrient intake and few studies adjusted for confounders, leading to potentially biased results. For example, a study by Harrison-Hohner and colleagues (61) derived the association between calcium and PPD from ancillary information in a study on calcium and preeclampsia. This type of secondary finding can provide information on a possible association between calcium and PPD, but it lacks the credibility of primary evidence of a randomized controlled trial or longitudinal cohort study. While the research has primarily examined the association of nutrition and PPD, no literature is currently available on the influence of maternal nutrition on antenatal depression. Thus, longitudinal studies with repeated measures are needed to determine whether poor nutrient status is associated with depressive symptoms in the antenatal period or the onset of depression in the postpartum period (4).

DIETARY INADEQUACY IN PREGNANT WOMEN

The link between nutrient deficiency and maternal depression in developed countries might not seem obvious. However, nutrient deficiencies among those who consume a typical western diet might be more common than people realize. A study of pregnant adolescents and adults living in the United States found mean intake for energy, iron, zinc, calcium, magnesium, folate, and vitamins D and E to be below recommended standards in both groups (8). Another study also found pregnant women did not consume adequate amounts to meet the nutrient requirements for calcium, iron, folate (94), n-3 essential fatty acids (94,95), and vitamin D (96) (see Figure 4). Even middle- to upper-income pregnant women did not consume adequate amounts of iron and possibly magnesium from foods (97). A British study found a high percentage of pregnant women did not meet the estimated average requirement (a nutrient intake value that is estimated to meet the requirement of half of the healthy individuals in a particular life-stage and sex group) for calcium (40%), iron (67%), and folate (69%) (98). Marchioni and colleagues found inadequate iodine intake in pregnant women, even though they lived in a region of Italy reported to have sufficient iodine levels available in their diets (9). A study of obese pregnant women found low status for a number of minerals in both the mother and their fetuses (99). Other studies have also found that pregnant women did not meet daily recommended intakes of nutrients through dietary means (8,60,97,98,100-102).

Given the evidence of dietary inadequacy in pregnant women and the link between nutrient deficiency and depression, it is reasonable to theorize about the potential influence of nutrient deficiency on the incidence of maternal depression. Proper nutrition during pregnancy is vital to the health of a woman and her fetus (103,104), as pregnancy presents unique stresses that challenge overall physical and psychological adaptation in women (105). Women are particularly vulnerable to the adverse effects of poor nutrition on mood because pregnancy and lactation increase nutrient requirements. It has been proposed by others that depletion of nutrient reserves throughout pregnancy and a lack of recovery postpartum may increase a woman's risk for maternal depression (4).

Author, year (reference)	Design and sample size (n)	Measurement	Outcomes	Limitations
Browne and colleagues, 2006 (93)	Prospective cohort, n=80 postnatal women, 41 diagnosed with depression, 39 controls	Screening used EPDS[a] and BDI[b]-II; diagnosis based on Composite International Diagnostic Interview; FFQ[c] collected during pregnancy	Prenatal fish consumption was not predictive of PPD[d], and postnatal n-3 status was not associated with PPD	Single FFQ and blood sample collected on fish consumption and PUFA[e] status; majority ate nonoily fish, which was not separated from oily fish consumption
De Vriese and colleagues, 2003 (68)	Cross-sectional study; n=48, 10 with PPD, 38 without	Blood samples extracted shortly after delivery and assayed for serum phospholipids and cholesteryl esters; interview used to assess for depression	Fatty acid concentration was lower in women with depression than in those not depressed	Cannot distinguish temporality: did low fatty acid precede depression or visa versa
Freeman and colleagues, 2006 (110)	RCT[f]: PPD women were randomized to take n-3 at 0.5 g/d (n=6), 1.4 g/d (n=3), or 2.8 g/d (n=7) for 8 wk	EPDS and HRSD[g] before and after treatment	Significant within group difference in pre- and posttreatment scores, ↓ 51.5% for EPDS, ↓ 48.8% for HRSD; no significant between group difference	Small sample size and lack of placebo group
Llorente and colleagues, 2003 (111)	RCT: breastfeeding women randomized to DHA[h] (200 mg/d) (n=44) or placebo (n=45) for 4 mos	Plasma phospholipid fatty acid patterns and scores on a self-rating questionnaire of current depression symptoms; a structured interview was used for depression in a subgroup	DHA serum levels were 8% higher in the treatment group and 31% lower in the placebo group; no difference between the two groups on self-rated or diagnosed depression	Small sample size; short duration; low DHA dosage
Makrides and colleagues, 2003 (112)	Cross-sectional cohort of 380 women	Completed an EPDS and had their iron, zinc, and DHA status assessed	For every 1% elevation in plasma DHA, there was 59% less symptom on the EPDS ($P<0.05$); plasma DHA positively influenced by maternal education and negatively associated with maternal smoking	Cannot distinguish temporality of association; one measure taken at 6 mos postpartum
Miyake and colleagues, 2006 (92)	Prospective cohort, n=865 pregnant women	Self-administered diet history questionnaire during pregnancy; depression screened with EPDS	No significant association found between dietary fish/fat intake and PPD	Wide range (2 to 9 mos) for postnatal screening; single self-administered semi-quantitative dietary questionnaire
Otto and colleagues, 2003 (113)	Prospective cohort, n=112 pregnant women	Venous blood samples were collected at wk 36 of pregnancy, after delivery, and 32 wks postpartum; PPD was assessed retrospectively at wk 32 after delivery, using EPDS	DHA was significantly lower in the "possibly depressed" group (EPDS≥10) compared with the not likely depressed group (EPDS<10)	Covariates associated with depression not considered by the authors in the analyses
Peet and colleagues, 1998 (70)	Cross-sectional study; n=30, 15 depressed, 15 controls	Measured fatty acid composition in depressed patients and controls	Depressed patients had significantly lower n-3 PUFA, DHA	Cannot establish temporal relationship; no control for covariates such as smoking, drug use, etc
Su and colleagues, 2003 (69)	RCT: double-blinded, placebo-controlled; n-3 PUFAs (9.6 g/d), for 8 wks; 22 depressed patients: 12 in treatment group, 10 placebo	HRSD	Patients in the n-3 PUFA group had a significantly decreased score on the 21-item HRSD compared to the placebo group	Small sample size and the possible confounding factor of uncontrolled combined medications
Su and colleagues, 2008 (73)	Second RCT: double-blinded, placebo-controlled trial with n-3 PUFAs (3.4 g/d) with placebo in pregnant women with major depressive disorder (*DSM-IV* criteria); n=6 randomly assigned, but n=24 finished study	HRSD as primary measure; EPDS and BDI were secondary measures	n-3 group had lower HRSD scores at wks 6 ($P=0.001$) and 8 ($P=0.019$), higher response rate (62% vs 27%, $P=0.03$),and lower depressive symptom ratings on the EPDS and BDI	Difference in response rate by group and possible unequal dropout rate associated with symptom severity; small sample size

[a]EPDS=Edinburgh Postpartum Depression Scale. [b]BDI=Beck Depression Inventory. [c]FFQ=food frequency questionnaire. [d]PPD=postpartum depression. [e]PUFA=polyunsaturated fatty acid. [f]RCT=randomized controlled trial. [g]HRSD=Hamilton Rating Scale for Depression. [h]DHA=docosahexaenoic acid.

Figure 3. Summary of studies on the association between n-3 fatty acid intake and maternal depression.

Author, year (reference)	Sample size	Measurement tool	Outcomes
Giddens and colleagues, 2000 (8)	59 pregnant adolescents and 97 pregnant adults	Two 7-day food records	Mean intakes for energy, iron, zinc, calcium, magnesium, folate, and vitamins D and E below recommended standards in both groups
Turner and colleagues, 2003 (97)	63 middle- to upper-income women	3-day diet records each month during pregnancy	Foods less than the EAR[a] were iron, magnesium, zinc, vitamin B-6, selenium, and vitamin C
Denomme and colleagues, 2005 (95)	20 pregnant women	Duplicates of actual foods eaten on 3 separate days (sent to laboratory for analysis) 3-day dietary record	PUFA[b] (65%) and DHA[c] (90%) levels below Acceptable Macronutrient Distribution Range
Mouratidou and colleagues, 2006 (98)	250 pregnant women	Interviewer-administered semi-quantified food frequency questionnaire	40% of participants did not meet the EAR for calcium, 67% for iron and 69% for folate
Sherwood and colleagues, 2006 (101)	61 pregnant women at 36 weeks, 60 lactating women	Weighed food records (for 3 days)	36% of pregnant women and 32% of lactating women did not meet folate requirements from dietary sources alone
Bodnar and colleagues, 2007 (96)	200 white and 200 black pregnant women	Serum vitamin D status measured at 4 to 21 weeks gestation and cord blood of neonates	Vitamin D–deficient[d] and insufficient[e] in 29.2% and 54.1% of black women and 45.6% and 46.8% black neonates, respectively; 5% and 42.1% of white women and 9.7% and 56.4% of white neonates were vitamin D–deficient and insufficient, respectively
Marchioni and colleagues, 2008 (9)	51 pregnant women, 100 age matched nonpregnant controls in Italy	UIC[f] in morning spot urine samples	UIC lower than adequate in 92% of pregnant women compared with 4% of controls ($P<0.001$)
Pinto and colleagues, 2008 (102)	240 pregnant women in Portugal	Food questionnaire	Low dietary intakes of vitamin E, folate, and magnesium both in the preconceptional period and during pregnancy, and low intake of iron during pregnancy

[a]EAR=estimated average requirements.
[b]PUFA=polyunsaturated fatty acid.
[c]DHA=docosahexaenoic acid.
[d]Deficient is defined as hydroxyvitamin D [25(OH)D]≤37.5 nmol/L.
[e]Insufficient is defined in this study as 25(OH)D<80 nmol/L; this cutoff correlates with a number of nutritional biomarkers that are impaired by inadequate vitamin-D status (96).
[f]UIC=urinary iodine concentrations.

Figure 4. Evidence of inadequate dietary intake in pregnant women.

CONCLUSION

The literature reviewed here suggests that nutrient intake can be a key factor in a woman's vulnerability to perinatal depression. There is a compelling argument for longitudinal research that targets this important topic as its primary focus: determining whether nutrient status is associated with maternal mental health in pregnant women.

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