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The role of maternal nutrition in the development and management of hydrocephalus in pregnancy: A narrative review

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Abstract

Maternal nutrition reflects the health and well-being of the fetus, making it one of the most critical and controllable factors in ensuring healthy growth and development throughout pregnancy. Therefore, deficiencies in certain nutrients during gestation could result in neurodevelopmental disorders like hydrocephalus. Hydrocephalus (HC) is a diverse condition marked by the accumulation of abnormal volumes of CSF within the brain's ventricles and subarachnoid space, contributing to approximately 276,000 neonatal deaths annually worldwide. Therefore, this review aims to analyze the role of maternal nutrition in the development and potential management of hydrocephalus during pregnancy. The search protocol involves searching these primary databases: PubMed, Cochrane Library, Google Scholar, and Research Rabbit supplemented by a manual search of references from selected relevant articles. Relevant articles that studied the relationship between maternal nutrition and congenital anomalies, multivitamin supplementation in pregnancy, the use of animal models to detect the development of hydrocephalus, and so on were reviewed. Relevant older articles were also included. It is concluded that maternal folic acid-fortified multivitamin supplementation during the periconceptional period is effective against the development of hydrocephalus. Multivitamin folic acid supplementation is recommended for women of childbearing age, whether or not, they are planning to get pregnant. Further research on the mechanism of how folic acid prevents congenital hydrocephalus should be explored.

Keywords: Hydrocephalus; Maternal Nutrition; Congenital Anomalies; Folic Acid; Multivitamin supplementation; pregnancy

1. Introduction

In the first nine months of gestation, a fetus's survival is tethered by a fragile connection—the umbilical cord—that links the fetus to the mother, who serves as its sole source of oxygen, waste removal, and, most critically, nutrition(1). The mother's body not only sustains but also nurtures the growth of the new human, supplying the nutrients essential for the transformation from a single cell into a complex organism of over 200 billion cells. In this crucial phase of intrauterine development, the fetus is shaped by two primary forces: heredity and environment. Heredity, determined at the moment of conception, sets the genetic blueprint for the individual and is beyond the reach of external influence(1). The environment, however, is a powerful and alterable force. For the fetus, this environment is the maternal body, and the state of the mother's nutrition directly affects fetal development. Maternal nutrition reflects the

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health and well-being of the fetus, making it one of the most critical and controllable factors in ensuring healthy growth and development throughout pregnancy(1).

Research from animal models and human studies across diverse nutritional contexts has established that maternal diet directly influences neurodevelopment, and malnutrition—whether undernutrition or overnutrition—can impair nutrient utilization. Given the rapid growth and high nutritional demands of fetal neurodevelopment, deficiencies in essential vitamins and minerals significantly increase the risk of congenital malformations and adverse pregnancy outcomes(2). Congenital anomalies contribute to approximately 276,000 neonatal deaths annually worldwide. Although the etiology of 50% of these anomalies remains unknown, identified factors include genetic, nutritional, infectious, and environmental influences, with maternal nutrition profile being a key determinant(3). One of the most common congenital anomalies is hydrocephalus(4).

A pathological enlargement of the cerebral ventricles, usually associated with elevated intracranial pressure, due to a disorder of the cerebrospinal fluid (CSF) physiology is generally referred to as Hydrocephalus (HC)(5). Hydrocephalus (HC) is a diverse condition marked by the accumulation of abnormal volumes of CSF within the brain's ventricles and subarachnoid space(6). The prevalence of this condition is about 1: 1000 children (7). Hydrocephalus is depicted by an active dilation of the brain's cerebral ventricles, caused by impaired cerebrospinal fluid (CSF) flow from its production site within the ventricles to its absorption point in the systemic circulation(8).

Naturally, cerebrospinal fluid (CSF) emanates from the lateral ventricles through the foramina of Monroe into the third ventricle. From there, it passes through the narrow aqueduct of Sylvius to reach the fourth ventricle. CSF exits the fourth ventricle via the paired lateral foramina of Luschka and the midline foramen of Magendie into the cisterns at the base of the brain. It then circulates through the cistern system posteriorly and over the convexities of the cerebral hemispheres (9). Hydrocephalus caused by an obstruction within the ventricular system is known as obstructive or non-communicating hydrocephalus. In contrast, hydrocephalus resulting from the obliteration of the subarachnoid cisterns or dysfunction of the arachnoid villi is non-obstructive or communicating hydrocephalus(9). Although hydrocephalus is one of the most prevalent congenital malformations of the central nervous system, its aetiology remains largely unexplained(10). Therefore, this review aims to analyse the role of maternal nutrition in the development and potential management of hydrocephalus during pregnancy.

1.1. Search Methods and Strategies for Research Identification

The search protocol involves the use of these primary databases: PubMed, Google Scholar, and Research Rabbit supplemented by a manual search of references from selected relevant articles. These databases were chosen for their extensive coverage of biomedical, clinical, and interdisciplinary research, ensuring a broad scope of relevant studies. Search terms included a combination of keywords related to maternal nutrition and pregnancy, such as "maternal nutrition," "pregnancy," "hydrocephalus," "micronutrient deficiency," "congenital malformations," "folic acid," and "neural tube defect". Boolean operators (AND, OR) were used to refine and expand the search, as needed.

1.1.1. Inclusion Criteria

- Peer-reviewed studies, reviews, and meta-analyses published within the last 20 years (a few of older articles that are very relevant were included).
- Research involving human subjects and/or relevant animal models.
- Studies that evaluate maternal nutrition and its influence on congenital anomalies, hydrocephalus in children; development and management of hydrocephalus; the role of nutrition in the development of abnormal pregnancy outcomes, etc.

1.1.2. Exclusion Criteria

- Articles not published in English.
- Studies unrelated to maternal nutrition or fetal neurodevelopment.
- Research centered on non-pregnancy-related hydrocephalus.

Finally, the references of selected articles were hand-searched to identify additional relevant articles that were not included in the initial search. This comprehensive approach ensured that the review incorporated a wide range of high-quality studies, offering a robust analysis of the role of maternal nutrition in the development and management of hydrocephalus during pregnancy.

2. Definition and Classification of Hydrocephalus

2.1. Definition of Hydrocephalus

Hydrocephalus is one of the most prominent congenital abnormalities of the central nervous system, characterized by abnormal accumulation of cerebrospinal fluid (CSF) within the brain's ventricular system. This pathology stems from disruptions in CSF dynamics, specifically an imbalance between its production at the choroid plexus and its subsequent absorption, leading to ventricular enlargement and increased intracranial pressure(4,11). A review published by Rekate H.L(8) defined hydrocephalus as: "an active distension of the ventricular system of the brain resulting from the inadequate passage of cerebrospinal fluid from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation". Hydrocephalus can be categorized as congenital, that which is present at delivery and acquired, that which develops later in life (4). Although some kinds of hydrocephalus can be seen at delivery, that are due to another problem. This kind of hydrocephalus remains unnoticed until aging or the pathology causes it to become symptomatic(11,12).

2.2. Etiology of Congenital Hydrocephalus

Congenital hydrocephalus (CH) encompasses a group of neurological disorders resulting from a disruption between cerebrospinal fluid (CSF) production and absorption, leading to its abnormal accumulation and increased intracranial pressure(13). Congenital hydrocephalus is described by the abnormal volume of cerebrospinal fluid (CSF) within the ventricular system, exerting pressure on the developing brain. If left uncared for, this disorder can result in different kinds of cognitive impairment like cerebral palsy, and visual deficits, with severe cases proving fatal(7). Congenital hydrocephalus (CH) encompasses a group of neurological disorders resulting from a disruption between cerebrospinal fluid (CSF) production and absorption, leading to its abnormal accumulation and increased intracranial pressure. The process by which congenital hydrocephalus progresses has not been well-established. However, it is assumed that it may develop at an important and specific embryonic gestational period of neural stem cell proliferation and differentiation in the brain (14). Congenital hydrocephalus can present either in isolation (non-syndromic) or as part of a syndrome involving other anomalies (syndromic) (15). In syndromic cases, identifying the specific defective gene is difficult due to the presence of multiple associated anomalies. Genetically, the isolated (non-syndromic) form is considered a primary condition, where hydrocephalus is the major phenotype caused by a single faulty gene(14).

There are various determinants of congenital hydrocephalus, some of which include aqueduct stenosis, Dandy-Walker malformation, and spina bifida. Additionally, numerous cases are linked to genetic factors, other malformations, post-infectious complications, or neoplastic conditions(15). A disruption of the neural cell membrane proteins crucial for brain development might be a probable cause contributing to the development of hydrocephalus (14). The L1 protein (essential for normal brain function and development), encoded by the X-linked hydrocephalus gene (L1CAM), belongs to the immunoglobulin superfamily of neural cell adhesion molecules and is expressed in neurons and Schwann cells. Hirschsprung's disease (HSCR), a condition marked by the absence of ganglion cells and the presence of enlarged nerve trunks in the distal bowel, has been associated with mutations in the L1CAM gene. Reports of patients with both X-linked hydrocephalus and HSCR, due to mutations in L1CAM, suggest that reduced levels of this protein may also contribute to the development of HSCR(14,16). Hydrocephalus may also result from a malfunction of the ependymal cells, with functional and morphological disturbances in these cells potentially leading to early ventricular dilatation before the development of aqueductal stenosis (14,17). A distortion in growth factor signaling pathways might result in hydrocephalus. The developmental abnormalities identified with congenital hydrocephalus indicate perturbations in critical signaling mechanisms involved in neurodevelopment, offering important insights into the underlying etiology of the condition(14,18). Hydrocephalus can also result from the disruption of key brain developmental patterning molecules during early neurodevelopment. While numerous genetic loci associated with hydrocephalus have been identified in animal models, providing valuable insights into the molecular etiology of the condition, genetic research on hydrocephalus in humans remains limited(14).

3. Risk Factors for the Development of Congenital Hydrocephalus in Pregnancy

3.1. Child-Related Risk Factors

3.1.1. Consanguinity

A study conducted by Ali et al(19) in Egypt found that children from families that are in consanguineous marriages have a higher risk of developing congenital hydrocephalus. To bolster this, in consanguineous families, gene mutations associated with the development of CH have been found, these include *L1CAM, AP1S2, MPDZ*, and *CCDC88C* mutations (20).

3.1.2. Family History of Hydrocephalus

A systematic review and meta-analyses conducted by Dewan et al(21) reported that there is a higher risk of CH if first- and second-degree family members suffer from CH(21). However, in a study by Ali et al(19), a family history of hydrocephalus was not found to be an independent risk factor in the development of CH.

3.1.3. Family History of Other Congenital Malformations

Families that have other CNS abnormalities like spina bifida might also suffer from CH(7). Increased risk of CH was also identified to be associated with children who suffer from other congenital malformations(19). Preterm infants also have an increased risk of occurrence of hydrocephalus(13).

3.2. Paternal Educational Status

Fathers with low levels of education have an increased risk of having offspring with CH(19). Illiteracy can limit the understanding of the concept of the fetus's condition and could limit the father from advising the mother on seeking antenatal care(22) And, the absence of adequate antenatal care increases the odds of CH(12).

3.3. Maternal Risk Factors

3.3.1. Maternal Age

A study reported by Yi et al. (13) on the prevalence of congenital hydrocephalus in Chinese newborns reported that mothers below 20 years of age had a higher risk of developing Congenital Hydrocephalus, as well as mothers aged 37 years and above(13). Also, a study conducted by Sipek et al.(23) in the Czech Republic reported that a higher occurrence of CH was discovered in mothers above 37 years of age(23). A study conducted in Denmark found that mothers under the age of 20 were more likely to have children with isolated hydrocephalus compared to those between the ages of 25 and 34(10).

3.3.2. Maternal Socio-Economics Status

Pregnant women with lower socio-economic and healthcare status were reported to have a high risk of occurrence of CH(19). That is, mothers with low socio-economic status are mostly low/unemployed, and have access to less antenatal care, which increases the occurrence of CH in their offspring(19). These mothers have lower odds of reporting serious illness during pregnancy(24).

3.3.3. Mother's Diseases during Pregnancy

Mothers who have experienced various ailments during pregnancy have increased odds of birthing children with CH(25). In one of these studies, the relationship between the diseases and CH was seen to be independent of medications used to treat these ailments during gestation. (25,26) Also, a study reported their findings showed that mothers who reported ailment during pregnancy have an increased risk of having offspring with CH(26).

3.3.4. Assisted Fertilization

A study conducted by Wennerholm et al(27) reported that children born after intracytoplasmic sperm injection (ICSI) have an increased risk of congenital anomalies only with multiple births, however, hypospadias was the only malformation that can be seen in excess in children after ICSI, which might be due to paternal infertility(27). Another study by Neumann et al(28) concluded that there was no higher risk of developing congenital head and neck defects in children conceived using assisted reproductive technology (ART) compared to children conceived naturally(28).

3.3.5. Previous Abortions

Musters et al(29) reported a relationship between previous abortions and hydrocephalus, that is, women with a prior history of abortions might have higher odds of giving birth to children with CH. However, in a study conducted by Ali et al, there was no significant positive association between women who have previously experienced abortion to delivering offspring with CH(19).

3.4. Maternal Nutritional Status

The significance of maternal nutritional factors gained relevance in the 20th century(30). Firstly, there was a study on how folic acid supplementation can be used to prevent and manage neural tube defects(31). And subsequently, research established the relation of low iron levels during pregnancy to maternal mortality, preterm birth, and birth developmental malformation(32). Therefore, it has been established that prenatal nutrition is crucial to fetal brain development(30).

Maternal malnutrition has been associated with the development of NTDs (Neural Tube Defects)(33). Through the epigenetics mechanism, maternal nutrition can modify gene expressions. For instance, the Methyl-donor micronutrients of the one-carbon metabolism, like choline, Vitamin B12, B6, and folic acid, are of significant value in the physiological developmental process, which can result in exposure or risk to neurodevelopmental anomalies(34). There could be the onset of the neurodevelopmental disorder and neurodegenerative ailments later in life if there were malnutrition during gestation and early life, which could result in the distortion of gene expression through epigenetic changes(35). Maternal nutrition plays a significant role in different stages(30):

- Before conception, adequate maternal nutrition is necessary to optimize nutritional status, uphold healthy fetal development, and provide support for the mother throughout pregnancy(36).
- At conception, adequate nutrition is relevant to support placenta growth and the gamete's function and health. For instance, rapid growth takes place in the first three weeks of conception. Where the brain undergoes different processes like apoptosis, synaptic formation, and neural migration. At this stage, any disturbances could subject the fetus to develop any neurodevelopmental malformation and neurodegenerative ailments later in adulthood(30).
- Maternal malnutrition during pregnancy is linked with cognitive disorders, motor defects, behavioral defects, neural tube defects, etc.

A result of a scoping review in 2021(2), that analyzed the relationship between maternal nutrition and neuro-development, categorized it into these classifications:

- Overall nutritional status of the mother, that is, overnutrition and/or malnutrition
- Macronutrients like protein and polyunsaturated fatty acids (PUFAs)
- Vitamins and Minerals like B12, A, B6, D, Choline, folic acids, etc.
- Other nutrients like Caffeine and gangliosides.
- Heavy metals(2).

The use of nutritional supplementation before and after conception by the mother plays a significant role in laying a healthy fetal brain development foundation, as well as being able to modify the brain through epigenetics mechanisms, which might lead to resistance to certain neurodevelopmental disorders(30). Moreso, maternal nutrition impacts signaling pathways, triggering epigenetic modification of fetus genes and affecting the development of the placenta, as well as nutrient transfer to the fetus(37).

3.4.1. Undernutrition

Deficiencies in certain nutrients pose the brain to some neurodevelopmental malformations as brain development makes use of about 75% of fetal energy(30). The results of undernutrition in pregnancy lead to different challenges based on the stage of gestation. At the early stage, it causes distortion in neuronal proliferation, and at the later stage, it causes distortion in neuronal differentiation(38). Deficiencies in some micronutrients like niacin, folic acid, vitamin A, and Zinc, could lead to congenital hydrocephalus(39).

3.4.2. Overnutrition

High-fat diet consumed during pregnancy could result in distortion of serotonergic and dopaminergic systems in the nucleus accumbens and ventral tegmental area, leading to higher odds of the fetus having neurodevelopmental and

behavioral disorders(40). The presence of obesity in mothers might make the offspring susceptible to the development of neurodegenerative disorders(41).

4. Key Nutrients and their role in the Development of Hydrocephalus

Richardson and Hogan were the ones to discover the possibility of hydrocephalus being caused by nutritional deficiency, by feeding the laboratory animal models with inadequate diet(42). To confirm this, Richardson and Demotter (43)fed the same diet to a different colony of rats. This diet is composed of "casein (acid washed), 25 grams; Cerelose, 57 grams; wood pulp, 3 grams; salts, 5 grams; lard, 10 grams; choline chloride: 0.1 gram; inosito1,P 0.01 gram; p-aminobenzoic acid: 0.05 gram; vitamin A, 3,000 I.U.; vitamin D, 425 I.U.;a-tocopherol: 2.5 mg.; Menadione," 2.5 mg.,; thiamine chloride: 1.0 mg.; riboflavin," 1.0 mg.; pyridoxine hydrochloride: 1.0 mg.; cdcium pant~thenate,~ 4.0 mg.; niacin: 5.0 mg.; and biotin: 0.02 mg"(42). They also discovered that some of the newborn of these animals had hydrocephalus(43).

4.1. Folic Acid

Folic acid is an essential intermediary in the synthesis of amino acids and nucleic acid. It is important in over 100 biochemical reactions and multiple regulatory pathways crucial for cellular function and development(44,45). Folic acid deficiency in pregnancy can be connected to distorted fetal brain development through incorrect DNA methylation(46). Adequate folic acid consumption in the maternal diet is necessary for neural cell proliferation, migration, differentiation, vascular transport, and synaptic plasticity. Folic acid has been shown to be effective against neural tube defects as it optimizes neurogenesis and axonal pro-regenerative effects as observed in animal models(47).

A study(31) conducted on the "prevention of neural tube defects" showed that folic acid supplementation can be used to avoid neural tube defects in children. In this study, a "significant 72% neural tube defects were prevented in the study group compared to the control group using folic acid (95% CI: 29% to 88%.) This study employed the use of a randomized double-blind design that excludes bias; therefore, the result can be considered accurate. This study also demonstrates that folic acid rather than any other vitamin was responsible for this effect(31). This study(19) also demonstrates that folic acid rather than any other vitamin was responsible for this effect. Moreso, The study on "Congenital Hydrocephalus (p-value 0.0001) and its Associated Risk Factors" reported that iron with folic acid supplementation in the early gestation period results in reduced risk of the development of congenital hydrocephalus in children(4). Furthermore, another study confirmed these findings, therefore, it can be concluded that there is an increased risk of developing CH in offspring if there is a maternal deficiency in folic acid.(19). There is about a 50% increase in the requirement of folic acid during pregnancy, and this can be achieved by taking folic acid supplementation of 400mg per day at preconception(44).

4.2. Vitamin B12

Vitamin B12 works as both an enzyme and a cofactor. It is relevant for hemoglobin generation, protein and fat metabolism, cytosol, methionine synthesis, etc(2). An adequate level of vitamin B12 in the maternal diet is necessary for optimal neural fetal development and myelination(48). Vitamin B12 deficiency in maternal nutrition below 200pg/mL has been linked with higher odds of the offspring having neural tube defects(44). There is a higher risk of vitamin b12 deficiency in pregnant women who practice vegan and vegetarian diets, because, this vitamin is mostly found in animal products(2). In addition, case reports of pregnant women with vitamin B12 deficiency showed that some of their children did not achieve optimal growth and development, showed irritability traits, and reduced cerebral growth. Maternal deficiency in vitamin B12 have been reported to be associated with congenital hydrocephalus(49).

Newberne and O'Dell(50) reported the occurrence in rats by giving them diets deficient in vitamin B12(51). In addition, a study on the "Relation of vitamin B12 and one-carbon metabolism to hydrocephalus stated that there was the occurrence of hydrocephalus in newborn animals after feeding their mother with a diet deficit of vitamin B12.(51). Dietary B-12 deficiency during embryonic and fetal development can lead to various developmental abnormalities, including hydrocephalus, abnormalities in the cerebral aqueduct such as closure, constriction, or irregular shape and size, partial or complete loss of ependymal cells in the third ventricle, and absence of specialized cell groups in the roof of the aqueduct and ventricles. Additional manifestations may include thyroid enlargement, edema, fatty degeneration of the heart, liver, and kidneys, as well as hemorrhaging in the yolk sac(49).

4.3. Vitamin A

Vitamin A (retinoic acid) and its derivatives are integral to neural patterning, neuronal differentiation, neurite outgrowth, and axonal elongation(52). It is primarily synthesized in the embryo; retinoic acid regulates the expression of crucial developmental genes and guides organogenesis(53). It is recommended for pregnant women to take 600 mg,

with key dietary sources including eggs, oily fish, fortified spreads, milk, and yogurt. Due to the teratogenic effects of vitamin A, high dosage should be avoided(54). In vitamin A-deficient rats, studies have highlighted the variability in both the intensity and distribution of nervous system lesions(55). Vitamin A deficiency in pregnant women can lead to the development of congenital hydrocephalus in the fetus. In contrast, Vitamin A in excess in nursing infants can lead to the development of acute hydrocephalus(49).

4.4. Vitamin B6

Vitamin B6 is found in both animal-based foods and vegetables, serving as a vital coenzyme in the metabolism of amino acids, carbohydrates, and fats. It plays a significant part in the development and maintenance of the central nervous system (CNS). In addition, Vitamin B6 is essential for serotonin synthesis and regulates mood, sleep, appetite, memory, and concentration. It also plays a crucial part in methylation processes, influencing gene expression and pathways critical to neurodevelopment and neurological function(34).

4.5. Vitamin D

Vitamin D modulates gene expression, impacting brain development. The recommended intake during pregnancy is currently 600 IU/day(30). Vitamin D modulates gene expression, impacting brain development. The recommended intake during pregnancy is currently 600 IU/day. Prenatal vitamin D deficiency could result in anomalies in brain development, distortions in neuronal differentiation and neurotransmission, modification in various signaling pathways and calcium homeostasis, and post-translational modifications, highlighting its crucial role in epigenetic regulation(56).

Vitamin D, when administered in average doses, can improve conditions like oligospermia; however, higher doses may lead to azoospermia. Excessive vitamin D, with excess vitamin A, has been implicated in cases of acute hydrocephalus accompanied by vomiting. Additionally, excessive vitamin D intake during pregnancy may result in placental calcification, leading to abortion, as well as renal damage in the offspring, manifesting as hematuria(49).

4.6. Zinc

Approximately 30% of the global population is estimated to have mild to moderate zinc deficiency. Plant-based diets cause zinc deficiency through two primary processes. First, they tend to provide lower dietary zinc intake, as meat and shellfish are the richest sources of this essential micronutrient. Second, the fiber and phytates found in plant-based foods inhibit zinc absorption(57). Zinc plays a significant part in fetal development, contributing to carbohydrate and protein metabolism, nucleic acid synthesis, and cellular division and differentiation(57). Research on animal models suggests that gestational zinc deficiency is associated with a significant reduction in the cerebellum, limbic system, and cerebral cortex, accompanied by a decreased cellular density in these critical brain regions(48).

4.7. Choline

Choline is primarily obtained from animal-based foods, with lesser amounts found in plant-based foods. Additionally, it can be synthesized internally in the maternal liver. Choline deficiency is prevalent, with estimates suggesting that approximately 90% of pregnant women in the United States fail to meet the recommended dietary intake levels(58). This micronutrient is involved in several biochemical and molecular pathways, including the formation of phospholipids and neurotransmitters. It serves as a methyl donor, facilitating epigenetic modifications in the fetal brain and placenta, and plays a role in stem cell proliferation and transmembrane signaling during neurogenesis(59). Choline plays a significant part in neurodevelopment, particularly in the adaptive modifications of cognitive functions. Consequently, maternal choline deficiency can disrupt neurogenesis and angiogenesis in the fetal hippocampus. Several studies suggest that oral supplementation of choline during the second trimester and after birth is related to improved sensory gating (56). The risk of neural tube defects in fetuses and maternal choline has been reported by some studies to be inversely related(30).

The study by Newberne et al.(60), aimed to examine the impact of severe and marginal deficiencies of lipotropes, particularly methionine and choline, on developing rat embryos. In this study, female rats were fed diets with varying levels of these nutrients. A diet low in choline and methionine, supported with vitamin B12, was marginally deficient yet supported normal conception, implantation, and fetal growth, preventing neonatal hydrocephaly. In contrast, without vitamin B12, even normal levels of choline and methionine resulted in congenital malformations and distortion of the nucleic acids and proteins in the brain and liver during different developmental stages. Although the marginally deficient offspring appeared clinically normal, biochemical analyses revealed smaller brain cells and irregularities in protein synthesis. These findings underscore the significant role of prenatal maternal nutrition in shaping neonatal outcomes, having a potential long-term effect on postnatal life(60).

4.8. Protein

Protein-energy malnutrition in fetal and early neonatal animal models leads to a reduction in neuronal DNA and RNA content and distorts the fatty acid profile(61,62). Fetal protein-energy malnutrition, often caused by maternal hypertension or severe malnutrition during pregnancy, could result in intrauterine growth retardation(63). Protein deficiency impairs hippocampal neurogenesis by reducing brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF), which in turn lowers the brain and neuronal volume. Furthermore, it lessens maternal lipid availability and fetal brain fatty acid levels, potentially limiting myelin production and heightening the risk of neurodevelopmental malformations(64). However, a direct link between protein deficiency and hydrocephalus have not yet been established, as the time of writing this review.

5. Management of Congenital Hydrocephalus with Maternal Nutrition

The use of folic acid-containing multivitamins by women of reproductive age before conception and continuing till the first three months after conception has been proven to reduce the risk of neurodevelopmental disorders in offspring, like neural tube defects, oral cleft, congenital hydrocephalus, etc(65). Apart from the known effect of periconceptional multivitamins against neural effects, generally, it also lowers the risk of incidence of other congenital anomalies(66). Periconception folic acid (FA) supplementation three months before the last menstrual cycle, and continuing till the end of the first trimester have been proven to be effective against congenital hydrocephalus in pregnancy. A study by Liu et al. on: "Folic acid supplementation and Risk of Congenital Hydrocephalus in China", suggested that FA supplementation during the periconceptional period was preventive against the development of CH in a fetus. That is, initiation at least 3 months before conception and continuation till the end of the first trimester is paramount because early termination and late start of FA supplementation have little to no effect against CH(67).

5mg or 400mg of daily supplementation of FA have been proven to be effective against congenital anomalies(68). Women should be counseled on sustaining a nutritionally adequate diet. However, FA multivitamin supplementation is required to meet the red blood cell folate level characterized by optimal protection against congenital anomalies like neural tube defects and hydrocephalus. Rich sources of folates in foods include oranges, spinach, peas, broccoli, etc(69). Folic acid food fortification on foods like cornmeal, flour and pasta should be considered. All women of reproductive age should be advised to take folic acid-containing multivitamins whether they are planning to get pregnant or not since most pregnancies are unplanned(69). Women of reproductive age should be counseled to take folic acid multivitamin supplementation including vitamins B12, and B, with eating choline-rich foods like egg yolk and meat(70).

6. Conclusion

Adequate maternal nutrition is crucial for optimal fetal development. Maternal nutrition plays a significant role in different stages of fetal development. For instance, a mother's diet before conception helps to optimize the mother's nutritional status, while that during conception helps to support healthy fetal development. It has been established that in the first three weeks of gestation, therefore, deficiencies of some certain nutrients expose the fetal brain to neurodevelopmental malformations, which could result in epigenetics changes. For instance, the methyl donor micronutrients of one-carbon metabolism like Choline, folic acid, vitamin B12, and B6, are of significant value in the physiological neurodevelopmental process, and deficiencies of these nutrients could result in neurodevelopmental disorders including congenital hydrocephalus.

Periconceptional folic acid-containing multivitamin supplementation has been proven to prevent congenital hydrocephalus. It is recommended that educational intervention of the use of multivitamins containing folic acid, zinc, choline, vitamin B12, and B6, in addition to consumption of a nutritionally adequate diet should encouraged to women of reproductive age, whether or not, they are considering pregnancy, since most pregnancy are unplanned. Provision of these vitamins should be made available at little to no cost, especially to the less privileged group. Further research on the mechanism by which folic acid is used in the prevention of CH should be explored further.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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