International Journal of Innovative Research in Engineering & Management (IJIREM)
ISSN: 2350-0557, Volume-9, Issue-1, February 2022
https://doi.org/10.55524/ijirem.2022.9.1.19
Article ID IJIR- IRP22917, Pages 110-115
www.ijirem.org

Homocysteine Role in Neural Tube Defect: A Review Paper

Krishan Raj Singh [1], and Dr. Arminder Kaur [2]

[1, 2] Assistant Professor, School of Applied Sciences, Sanskriti University, Mathura, Uttar Pradesh

Correspondence should be addressed to Krishan Raj Singh; hodbio-tech@sanskriti.edu.in

ABSTRACT: Folic acid, when administered periconceptionally, is now well recognized as having the potential to prevent a variety of neural tube disorders. Folic acid seems not to treat a nutritional deficiency in pregnant women, according to a recent research. Rather, it seems that these neural tube anomalies are caused by a metabolic flaw or errors, which may be corrected with enough folic acid. Folic acid seems to have the most influence on homocysteine metabolism, according to a new research. We observed that moms who were carrying diseased fetuses had much greater homocysteine levels than those who were not. These data suggest that one of the enzymes involved in homocysteine metabolism is likely to be aberrant in afflicted pregnancies. The conversion of homocysteine to methionine may be the essential stage, according to animal research. In cultured rat embryos, methionine is necessary for neural tube closure. Homocysteine metabolism necessitates the enzymes methionine synthase, cystathionine synthase, and 5, 10 methylene tetrahydrofolate reductase. If methionine synthase is the dominant enzyme, vitamin B-12, such as folic acid, has a higher chance of activating the aberrant enzyme, posing a public health risk. Vitamin B-12 may find things simpler to limit the amount of folic acid in fortified foods, reducing the risk of folic acid overdose.

KEYWORDS: Birth Defect, Folic Acid, Folate, Homocysteine, Neural Tube Defect.

1. INTRODUCTION

Homocysteine is a typical amino acid in your blood. It is mostly obtained from eating meat. Abnormal amounts of it are connected to early improvement of coronary illness. Homocysteine is a -amino corrosive that is not proteinogenic. It is a homologous of the corrosive amino cysteine, but with the addition of a methylene connective (-CH2-). The clearance of methionine's terminal C methyl gathering biosynthesizes it. With the help of some B-nutrients, homocysteine can be converted to methionine or cysteine. Hyperhomocysteinemia (high homocysteine levels in the blood) makes a person more prone to endothelial cell loss, which produces vein pain and may develop to atherogenesis, which can cause ischemia damage. As a consequence, hyperhomocysteinemia may be a risk factor for coronary supply-chain illness. Coronary vein disease arises when an atherosclerotic plaque restricts blood flow to the coronary conduits, which supply oxygenated blood to the heart. Although hyperhomocysteinemia has been related to blood clots, heart attacks, and strokes, it is uncertain if the condition is a risk factor in and of itself. Hyperhomocysteinemia also has been linked to miscarriage and neural tube defects in the early stages of pregnancy. The architecture of homocysteine as a Zwitter ion at neutral pH is seen in Figure 1[1].

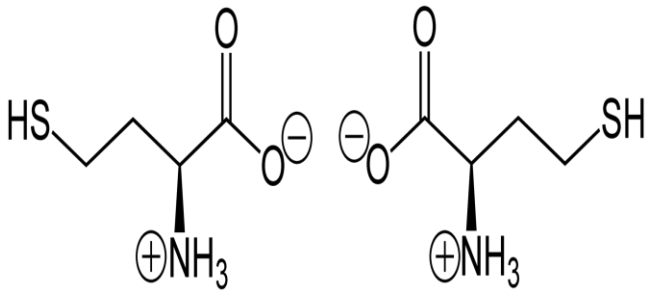

Figure 1: Structure of Homocysteine exists at a neutral pH value as a zwitter ion [2].

A. Biosynthesis and Biochemical Roles

Homocysteine does not come from food. Instead, a multi-step procedure is used to biosynthesize it from methionine. To begin, ATP provides methionine with an adenosine bunch, which is subsequently transformed to S-adenosyl methionine by S-adenosyl-methionine synthetase (SAM). The methyl gathering is transported to an acceptor particle by SAM (e.g., norepinephrine as an acceptor during epinephrine union, DNA methyltransferase as a halfway acceptor during the time spent DNA methylation). L-homocysteine is generated when adenosine is broken down. Tetrahydrofolate (THF) converts L-homocysteine back into L-methionine, and L-cysteine is converted back into L-methionine [3].

B. Biosynthesis of Cysteine

Warm blooded animal's biosynthesize the amino corrosive cysteine by means of homocysteine. Cystathionine-synthase catalyzes the formation of cystathionine from homocysteine and serine. Pyridoxine (vitamin B6) is used as a cofactor in this reaction. This twofold amino corrosive to cysteine, smelling salts, and -ketobutyrate is then believed by

cystathionine-lyase. Microscopic organisms and plants, which rely on O-acetylserine for cysteine production, use a different mechanism[4].

C. Methionine Salvage

Methionine may be made from homocysteine. The methyl giver is N5-methyl tetrahydrofolate, and the cobalamin (vitamin B12)-related molecules are used in this method. The page on methionine synthase has further information on these catalysts[5].

D. Other reactions of biochemical significance

Homocysteine thiolactone, a five-membered heterocycle, may cyclize to produce homocysteine thiolactone. Homocysteine-containing peptides will generally separate themselves by oxidative stress reactions as a consequence of this "self-circling" response [6]. At Dopamine D2 receptors, homocysteine functions as an allosteric antagonist. Homocysteine and its thiolactone are thought to have had a role in the early development of life on Earth.

II. LITERATURE REVIEW

M J Adams Jr explores the impact of folic acid on neural tube defects protection (NTDs). The defence mechanism, on the other hand, is already being developed. A case-control research was conducted to investigate the role of folate and cobalamin-related substances in the development of NTDs. Gas chromatography/mass spectrometry was used to measure the concentration of folate, cobalamin, and 14 other connected metabolites in midtrimester serum samples from 32 women with NTD-affected childbirth and 132 control women, and also serum specimens from 46 nonpregnant individuals with a history of NTD-affected pregnancy and 43 nonpregnant control women. In both the midtrimester and nonpregnant groups, the log-transformed average of metabolites was compared between case and control women. Case women in the pregnant group had higher blood methylmalonic acid (MMA) levels than dominant women (130 vs 105 nM) (130 vs 105 nM). Women with MMA levels above the 90th percentile had a 13-fold increased relative risk of an NTD-affected pregnancy, showing a dose-response relationship between midtrimester serum MMA levels and the risk of an NTD-affected pregnancy. There was no difference in serum MMA levels between control and test women in the non-pregnant group (140 vs 140 nM) (140 vs 140 nM). In the midtrimester, women whose pregnancies were not disturbed by NTDs had considerably lower serum MMA levels than nonpregnant women, but women whose pregnancies were disrupted by NTDs had levels equivalent to nonpregnant women. Greater MMA serum concentrations in NTD-affected pregnant women in the midtrimester imply that cobalamin may have a part in the development of NTDs. More research is required to identify the role of cobalamin in folic acid's protective properties[8].

C Bower's study compared women who had originally provided birth to a child with a neural tube defect to mothers who had no children with this condition in terms of their capacity to hydrolyze and digest pteroylpolyglutamates (PteGlun) present in a routine meal. Case mothers had significantly lower baseline blood and erythrocyte folate contents, but also smaller increases in serum folate after the PteGlun meal, as compared to control women who worked at the research site where the trial was performed. When case moms were compared to a group of mothers who were acquaintances of the case moms, all folate estimations were identical. The greater the baseline serum and erythrocyte folate concentrations, the greater the increase in serum and erythrocyte folate immediately after the test meal, according to the data. The coefficients for creating a model for the serum folate frequency response vary significantly between case and control mothers. Regardless of the fact that the response curves for the two groups vary considerably, we conclude that intestinal hydrolysis of PteGlun administered orally is unaffected in women who have given birth to children with neural tube abnormalities when compared to controls with comparable baseline folate levels. More research is required to determine what is driving this disparity[9].

Headfold-stage rat embryos fed on cow serum without extra methionine failed to form neural tubes, lacked eyes and branchial arches, were abnormally shaped, and also had lower strength than methionine-supplemented embryos, according to C N Coelho's research. Methionine was particularly significant in supplemented cultures during first 18 hours of culture, when neural tube closure began. In any of the cow serum samples examined, no other amino acids or vitamins, including folate, were found to be viable substitutes for methionine. At quantities of at least 500 micrograms/ml, methionine had no impact on cultured rat embryos Cow serum contained less free methionine than rat serum, and cow serum proteins had considerably less methionine relative to other amino acids than rat serum proteins, according to serum free amino acid analyses. Cow serum dialysis reduced but did not eliminate the requirement for methionine. This meant that either the free amino acids in bovine serum were out of balance or that a dialyzable component in the serum was interfering with methionine ownership and usage. Even when no additional methionine was given, food supplementation with rumen-protected DL-methionine increased serum methionine levels in cows, and blood taken from treated cows preserved normal rat embryo development[10].

III. DISCUSSION

A. Homocysteine Levels

Homocysteine levels in males are typically greater than in women, and they rise with age. Western people have dimensions of 10 to 12 mol/L, but groups with low B-nutrient diets or the elderly have dimensions of 20 mol/L. (e.g., Rotterdam, Framingham)[6].

B. Elevated Homocysteine

Hyperhomocysteinemia is a disorder in which blood homocysteine levels are unusually high, reaching 15 mol/L. This has been related to a variety of illnesses, including thrombosis, neuropsychiatric problems, and fractures. It's also linked to microalbuminuria, which is a good indicator

of future cardiovascular disease and renal impairment. When paired with high blood folate levels, insufficient vitamin B12 levels have been associated to an increase in homocysteine fixations in general[8].

C. Neural Tube Defects (NTDs)

NTDs (neural tube defects) are a kind of birth abnormality in which a gap develops in the spine or brain early in human development. During the third seven days of pregnancy, certain cells on the developing organism's dorsal side begin to change shape and build the neural cylinder, a process known as gastrulation. An NTD arises when the neural cylinder fails to close entirely. Explicit forms include spina bifida, which affects the spine, anencephaly, which impairs mental function, encephalocele, which affects the skull, and iniencephaly, which affects the neck. NTDs are one of the most well-known birth abnormalities, impacting around 300,000 infants each year throughout the globe. In the United States, roughly 1,500 kids are born with spina bifida each year, or about 3.5 in 10,000 (0.035 percent of all births), compared to about 5 in 10,000 (0.05 percent of all births) before grain diets became folate-rich. The number of mortality in the United States owing to neural cylinder deserts has fallen from 1,200 in the year before the folate fortress was formed to 840 in the year after[4].

D. Types of Neural Tube Defects

Open and closed NTDs are the two types of NTDs. Open NTDs make progress toward normalcy. Open NTDs develop when the brain and spinal cord are revealed after birth due to a deformity in the skull or vertebrae (spines). Open NTDs include anencephaly, encephaloceles, hydranencephaly, iniencephaly, schizencephaly, and spina bifida. Shut NTDs are a type of NTD that is less prevalent. When a spinal defect is fixed by skin, it is referred to as a closed NTD. Lipomyelomeningocele, lipomeningocele, and fastened line are common examples of closed NTDs[6].

a. Anencephaly

Anencephaly is the lack of a significant portion of the cerebrum, skull, or scalp during embryonic development. Between the 23rd and 26th day after conception, the rostral (head) side of the neural cylinder fails to develop, resulting in a cephalic issue. Although it is widely recognized that children born with this condition lack a telencephalon, which is the largest chunk of the cerebrum and primarily consists of the cerebral halves of the globe, like the neocortex, which is responsible for perception, the Greek expression literally translates to "no in-head" (that is, a complete lack of internal head parts such as the mind). Because the structure lacks skin, bone, meninges, and other tissues, it is held together by a thin layer of film. In a tiny percentage of instances, newborns born with this condition do not survive and over a few hours, if not days, after being born. As a consequence, anencephaly (lack of cerebrum) is a neural tube defect that develops between the 23rd and 26th weeks of pregnancy when the head end of the neural tube shuts, resulting in the loss of a significant section of the mind and skull. Babies born with this condition are blind, deaf, and illiterate because the primary part of the forebrain—the most critical component of the cerebrum—is missing. The newborn kid will never learn to reason since he or she lacks a functioning cerebrum. Newborn newborns are either stillborn or die shortly after delivery, usually within a few hours or days[2].

b. Encephaloceles

Encephalocele is a malformation of the neural cylinder that is characterized by sac-like bulges in the mind and a film that spreads it via perforations in the skull. These abnormalities are caused by the failure of the neural cylinder to fully close during embryonic development. A score going down the middle of the head, between the temple as well as the nose, or just on the back of the head indicates encephaloceles. The severity of an encephalocele is determined by its location. As a consequence, encephaloceles are classified as film-bound sac-like protrusions of the mind through the skull. They might be a furrow running along the center of the top half of the head, between both the brow and the nose, or a furrow running down the back. Encephaloceles are frequently evident and may be detected promptly. Little encephaloceles in the nasal opening and temple are sometimes missed[1].

c. Hydranencephaly

In hydranencephaly, the cerebral halves of the head are absent to a large extent, and the remaining cranial space is filled with cerebrospinal fluid. The disorder hydranencephaly affects the brain. These strews are natural illnesses that occur when the embryonic sensory system is damaged or develops abnormally during the most important periods of prenatal development. The logical phrase for "head" or "head end of body" is cephalic. They are connected to a variety of genetic or inherited disorders, as well as natural circumstances such as maternal disease, medication admission, or even high amounts of radiation exposure. This is not to be confused with hydrocephalus, which is caused by an excess of cerebrospinal fluid accumulating in the brain's ventricles. Only half of the cranial pit is affected by hemihydranencephaly. As a result, hydranencephaly occurs when the cerebral sides of the equator are missing and substituted by cerebrospinal fluid sacs[4].

d. *Iniencephaly*

Iniencephaly is an uncommon kind of cephalic disorder first reported in 1836 by Étienne Geoffroy Saint-Hilaire. The term is derived from the Greek word "inion," which meaning "neck scrape." The occipital bone deficiency, cervical spina bifida, and retroflexion (reverse bending) of the head on the cervical spine are all frequent in persons suffering from the condition. With the exception of a few rare instances of live delivery, the most common result is stillbirth, which is invariably followed by death within a short amount of time. As a consequence, iniencephaly is an uncommon neural cylinder deformity characterized by extreme head-to-spine twisting. Because the head is tilted backwards and the face faces upwards during prenatal ultrasound screening, the finding is generally made, but if it isn't, it will almost certainly be discovered after birth. In the

great majority of instances, the neck is missing. Face skin is inextricably linked to the chest, and scalp skin to the upper back. The infant will only live for a few hours in the great majority of situations[6].

e. Spina bifida

The spine and the layers covering the brain and spinal cord are shattered in spina bifida, a birth disorder in which the spine and the layers surrounding the brain and spinal cord are fractured during early development. The three most common types are spina bifida occulta, meningocele, and myelomeningocele. The lower body is the most well-known, although the middle or upper back might also be affected in rare situations. There really are no or very modest signs in Occulta. A shaggy fix, a dimple, a dull area, or swelling on the back surrounding the opening in the spine might all be signs of Occulta. Meningocele is a disorder in which a sac of liquid develops near the spine's entrance, resulting in minor symptoms. The most dangerous kind is myelomeningocele, sometimes known as open spina bifida. Poor walking skills, bladder or bowel control troubles, liquid buildup in the cerebrum (hydrocephalus), a tight spinal line, and latex sensitivity are all linked to this illness. Learning issues are rather common. Spina bifida is caused by a combination of genetic and environmental factors in most cases. After having one child with the illness or if one of the guardians has the illness, there is a 4% risk that the next child will be afflicted. A lack of folate in the diet before to and during pregnancy is also a contributing factor. Other risk factors include some anti-seizure medications, obesity, and poorly controlled diabetes. A diagnosis might be established before or after the birth of a child. There is an increased likelihood of spina bifida if a blood test or amniocentesis reveals an abnormal condition of alpha-fetoprotein (AFP) before delivery. An ultrasound scan may also reveal the problem. Medical imaging may be used after the infant is delivered to confirm the diagnosis. Anencephaly and encephalocele are two forms of neural cylinder abnormalities that may be separated from spina bifida. The majority of spina bifida cases may be averted if a woman gets enough folate before and throughout her pregnancy. The majority of women have been proven to benefit from adding folic acid to flour. Spina bifida may be closed exactly before or after delivery. In individuals with hydrocephalus, a shunt may be necessary, and a knotted spinal rope may need to be carefully mended. Devices that aid development, such as supports or wheelchairs, may be beneficial. Catheterization of the urinary tract may also be required.

Around 15% of the population is affected with spina bifida occulta. Spina bifida prevalence varies widely by nation, ranging from 0.1 to 5 per 1000 births. In wealthy nations, such as the United States, it affects around 0.4 out of every 1000 babies. In India, it affects around 1.9 out of every 1000 infants. Caucasians, as compared to Black people, are at a higher risk. The term "split spine" is Latin in origin. As a consequence, there are two subtypes of spina bifida: cystica and occulta spina bifida.[10].

f. Spina bifida cystic

There are two forms of meningocele: meningocele and myelomeningocele. Meningocele is a less serious disorder in which the meninges protrude through the opening in the spinal channel but not the spinal string. The most basic variety of spina bifida is a back meningocele, often known as a meningeal pimple. The meninges may herniate between the vertebrae due to a single developmental fault in this structure. Despite reports of twisted lines, persons with meningocele are unlikely to have long-term medical issues as long as their sensory system is intact. Meningocele may be caused by teratoma, different sacrococcyx and presacral cancers, and Currarino disease.

A meningocele may also be caused by a dehiscence near the base of the skull. There are three types of these: occipital, frontoethmoidal, and nasal. The tip of the nasal pit produces endonasal meningocele, which might be mistaken for a nasal polyp. They're handled with care. In that they both include cerebrum tissue, encephalomeningoceles and encephalomeningocele are similar. Myelomeningocele is characterized by the herniation of the meninges as well as the passage of the spinal string through the hole. Myelomeningocele (MMC), also known as meningomyelocele, is a kind of spina bifida that causes major difficulties by damaging the meninges and nerves. The injectable component of the spinal segment allows the spinal line to distend through an opening in persons with myelomeningocele. Myelomeningocele arises when the neural cylinder pore closes during the third seven days of embryonic development. The fact that what has transpired is a huge disappointment for MMC. The meningeal films that convey the spinal rope distend into the hole, forming a sac that encases the meninges, cerebrospinal fluid, and sections of the spinal line and nerve roots[9].

g. Spina bifida occulta:

The term occulta comes from the Latin word occultus, which means "hidden." This is the least severe kind of spina bifida. A portion of the exterior component of the vertebrae isn't completely closed in occulta. The spinal line doesn't really protrude because the vertebral components are so small. The skin around the injured site may be normal or have hair growing through it; it may also have a dimple or a birthmark. Spina bifida occulta, unlike most other types of neural cylinder surrenders, isn't related with an increase in AFP, a typical screening test for detecting neural cylinder relents in utero. Unlike the vast majority of prior neural cylinder surrenders, the dural covering is preserved in this instance.

Because this kind of spina bifida is frequently asymptomatic, many persons with it are ignorant that they have it. Around 15% of the population has spina bifida occulta, and the vast majority of cases are detected by coincidence using spinal X-rays. A careful review of the data of radiographic investigations revealed no relationship between occult spina bifida and back pain. The audit's unfavorable results are bolstered by other late investigations that were not included in the report. In any case, some research imply that spina bifida occulta isn't necessarily a benign condition. According to one research, patients with

spina bifida occulta are more severely impacted by back discomfort. It's possible that this is confused with dysmenorrhea in women.

Although a deficient back combination is not genuine spina bifida, it may have neurological consequences. The meninges do not herniate through to the gap in the spinal canal when the neural cylinder is destroyed. Spina bifida occulta is the medical term for a hidden divided spine. Spina bifida occulta occurs when sections of the spine's bones, known as the spinous procedure, and the neural curve seem abnormal on a radiogram without the spinal string and spinal nerves. Persons with a first degree relative had a 5–10 times increased likelihood of repeating than those without (parent or kin)[10].

E. Causes

a. Folate deficiency

During pregnancy, a lack of folate (vitamin B9) and nutrition B12 has been linked to an increased risk of NTDs. Despite sharing the same biopathway, folate deficiency is significantly more common and hence a higher concern. Folate is necessary for cell formation and maintenance, and also the mixing of DNA and RNA. Folate is suggested to help with methylation and possibly damaging nucleic acid pairings by transferring one carbon group. It has been hypothesised that the early human foetus is particularly vulnerable to folate deficiency due to differences in the valuable compounds in this pathway during embryogenesis, and also a strong interest in post translational methylation of the cytoskeleton in neural cells during neural cylinder closure. Failure to methylate the post-translational cytoskeleton, which is essential for separation, has been linked to aberrant neural cylinders. Because vitamin B12 is such an important receptor in the folate biopathway, research has shown that it increases the incidence of NTDs. Despite the fact that dihydrofolate reductase activity varies in the human liver, there is good evidence that fast folic supplementation raises blood levels of bioavailable folate. A high-folate diet (350 g/d) may offer the same rise in plasma folate as low-dose folic acid (250 g/d) in adults. A cross-national research of all-inclusive community results utilizing several techniques to encourage folate intake, on the other hand, revealed that a single general nutrition diet with folic corrosive reduces neural cylinder abnormalities. While there has been some concern that folic acid supplementation is linked to an increased cancer risk, a 2012 research found no evidence that shows a minor reduction in risk, with the exception of prostate illness[5].

F. Gene-environment interaction

The loss of neural cylinders is not caused by a shortage of folate. A quality situation connection, such as defenselessness produced by the C677T Methylenetetrahydrofolate reductase (MTHFR) mutation, is responsible for the correlation between folic acid corrosive supplementation and fewer neural tube defects. Increased folic acid during pregnancy lowers the incidence of NTDs by preventing this generally sub-clinical sensitivity to irritating situations. Antimetabolites of folate (such as methotrexate), mycotoxins in deteriorated maize meal, arsenic, early-onset hyperthermia, and radiation are also potential causes. Maternal obesity has also been linked to the development of NTDs. Both mother cigarette smoking and maternal secondhand smoke exposure, according to research, increased the incidence of neural tube abnormalities in kids. According to a few research that reveal a relationship between cigarette smoking and homocysteine levels, maternal tobacco smoke exposure may raise the risk of NTD in future generations. Ingestion of cigarette smoke during pregnancy raises the chance of neural tube defects. Because neural tube defects are linked to a variety of traits, all of the following may work by preventing distinct components of correct folic corrosive digestion and folate-related methylation-related cell forms[4].

G. Diagnosis

The neural cylinder is examined using ultrasound and maternal blood alpha-fetoprotein levels are measured to search for abnormalities (MSAFP). Ultrasonography is the major screening tool for NTDs in the second trimester, with MSAFP as a supplemental screening test. This is related to higher wellbeing, better affectability, and a decreased ultrasound false positive rate when compared to MSAFP. To establish if ultrasound screening indicates a positive risk, amniotic liquid alpha-fetoprotein (AFAFP) and amniotic liquid acetylcholinesterase (AFAChE) testing are utilized. Despite the fact that more serious abnormalities may not be identified until later in life, these deformities are often obvious right after birth. Despite the fact that a raised MSAFP at 16–18 weeks of development is a powerful indicator of open neural cylinder abandons, the test does have a high false positive rate (2 percent of all women tested in Ontario, Canada between 1993 and 2000 tested positive without having open neural cylinder deformity, despite the fact that 5% is the most commonly cited result worldwide), and only a few neural cylinder deformations are characterized by this screen test (73 percent in a similar Ontario study). Despite the fact that the site of ultrasonography is subject to administrative preparations and the nature of the equipment, MSAFP screening in conjunction with regular ultrasonography has the greatest detection rate[3].

H. Prevention

In 1996, the US Food and Drug Administration required folic acid to be added to advanced breads, oats, wheat, and other grain products. It's important to remember that the neurulation process needs enough folate to work correctly for most of the first month of pregnancy (when most women aren't even aware they're pregnant). To lower the chance of real birth defects, women who may become pregnant are urged to eat folic acid-fortified meals or supplements in addition to folate-rich foods. In Canada, mandatory folic folate fortification of certain diets has been proven to lower neural cylinder absconds by 46 percent. Women who are attempting to conceive are advised to take 400 micrograms of folic acid per day. In the United Kingdom, women who have just given birth to a child with a neural cylinder defect may benefit from taking a daily dose of 4.0 mg/5.0 mg as prescribed by their doctor[7].

Since 2008, NTD drugs have been based on the severity of the problem. Anencephaly has no therapy, and newborns usually don't live more than a few hours. Survival and elements of newborns with spina bifida, meningocele, and mellow myelomeningocele have improved thanks to forceful, meticulous administration. Medical methods are often determined by the quantity of cerebrum tissue involved with an encephalocele. The purpose of NTD treatment is to let the person to reach their maximum level of capacity and autonomy. A fetal medical surgery was conducted before 26 weeks of incubation in the hopes of improving the end result, which included a decrease in Arnold–Chiari mutation and hence the need for a ventriculoperitoneal shunt. The method, on the other hand, is very risky for both the mother and the baby, and it is frequently seen as intrusive, with fears that the positive results are attributable to a genetic predisposition. Further, this medical procedure isn't a remedy for all issues related with a neural cylinder imperfection. Different regions of research incorporate tissue designing and undifferentiated organism treatment however this examination has not been utilized in people [6].

IV. CONCLUSION

Our new study shows a substantial increase in Homocysteine in mothers bearing an afflicted fetus. Earlier study in the same cohort demonstrating that B12 was an independent risk factor pointed to methionine synthase as the key enzyme. Although animal work supports this connection, animal metabolism is not always comparable to human metabolism. Thus, additional study must be done to validate or reject the methionine synthase hypothesis. The methionine synthase theory has intriguing public health implications. If an aberrant enzyme is responsible for NTDs, it may be feasible to stimulate this enzyme not just with folie acid but with B-12 as well. If this were true, it might decrease the amount of folie acid needed to a level that could be placed into fortified foods without generating concerns about overexposure in the general population.

REFERENCES

[1] “Economic Burden of Spina Bifida—United States, 1980-1990,” Clin. Pediatr. (Phila)., 1990, doi: 10.1177/000992289002900318.

[2] I. D. A E Czeizel, “Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation,” N. Engl. J. Med., vol. 327, p. 4, 1992.

[3] C. Bower, F. J. Stanley, M. Croft, N. H. De Klerk, R. E. Davis, and D. J. Nicol, “Absorption of pteroylpolyglutamates in mothers of infants with neural tube defects,” Br. J. Nutr., 1993, doi: 10.1079/bjn19930083.

[4] C. N. D. Coelho, J. A. Weber, N. W. Klein, W. G. Daniels, and T. A. Hoagland, “Whole rat embryos require methionine for neural tube closure when cultured on cow serum,” J. Nutr., 1989, doi: 10.1093/jn/119.11.1716.

[5] D. L. ECONOMIDES, J. FERGUSON, I. Z. MACKENZIE, J. DARLEY, I. I. WARE, and M. HOLMES-SIEDLE, “Folate and vitamin B12 concentrations in maternal and fetal blood, and amniotic fluid in second trimester pregnancies complicated by neural tube defects,” BJOG An Int. J. Obstet. Gynaecol., 1992, doi: 10.1111/j.1471-0528.1992.tb14386.x.

[6] P. Gardiki-Kouidou and M. J. Seller, “Amniotic fluid folate, vitamin B12 and transcobalamins in neural tube defects,” Clin. Genet., 1988, doi: 10.1111/j.1399-0004.1988.tb03478.x.

[7] J. E. Haddow, L. E. Hill, E. M. Kloza, and D. Thanhauser, “NEURAL TUBE DEFECTS AFTER GASTRIC BYPASS,” The Lancet. 1986, doi: 10.1016/S0140-6736(86)91252-3.

[8] S. Kumar, J. R. Foreman, and M. Rathi, “Amniotic fluid and maternal serum amino acid levels in malformations of fetal central nervous system,” Neurochem. Res., 1980, doi: 10.1007/BF00964233.

[9] M. J. Landon, D. H. Eyre, and F. E. Hytten, “TRANSFER OF FOLATE TO THE FETUS,” BJOG An Int. J. Obstet. Gynaecol., 1975, doi: 10.1111/j.1471-0528.1975.tb00556.x.

[10] . P. S. M J Adams Jr , M J Khoury, K S Scanlon, R E Stevenson, G J Knight, J E Haddow, G C Sylvester, J E Cheek, J P Henry, “Elevated midtrimester serum methylmalonic acid levels as a risk factor for neural tube defects,” Teratology, vol. 51, p. 7, 1995.