

Role of Vitamin B12 and Folic Acid in Obsessive-Compulsive Disorder: Review Article

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ABSTRACT

Background: When a person suffers from obsessive-compulsive disorder (OCD), they experience intrusive and disturbing thoughts about specific topics (known as "obsessions") or feelings of compulsion to perform specific behaviors (known as "compulsions"). There is mounting evidence that dietary folate and vitamin B12 are crucial to the normal and abnormal functioning of the neuropsychiatric system. Studies on the incidence of neuropsychiatric symptoms in patients deficient in vitamin B12 have been conducted all over the world. Folate and vitamin B12 have lately been described in a substantial amount of literature as therapy or supplements for the management of psychiatric diseases.

Aim of work: Shedding the light on the role of vitamin b12 and folic acid in OCD cases hoping to improve lately the assessment of symptoms severity and thus reducing the morbidity and mortality rates.

Methods: Our research was a review article, interpreted in Al-Azazy Mental Health and Addiction Treatment Hospital during the period from august 2022 till January 2023. The Zagazig University IRB (ZU-IRB #9456/10-4-2022) was contacted for approval. We compiled and evaluated data from a wide range of relevant studies before writing a narrative review of our findings.

Conclusion: We came to the conclusion that certain neuropsychiatric illnesses, such as OCD, can be correlated with vitamin B12 and folic acid levels. We suggest keeping a close eye on this phenomenon, which has to be investigated further. Our results can be used as a jumping off point for related studies.

Keywords: Obsessive, Compulsive, Vitamin B12, Folic acid.

INTRODUCTION

Vitamins B12 and folic acid are examples of water-soluble vitamins. Both are critical for making new RBCs, but vitamin B12 is especially important for keeping the brain and nervous system healthy. Mood disorders, dementia, paranoid psychoses, violent behavior, and demyelinating myelopathy are only some of the psychiatric and neurological problems that have been associated to vitamin B12 and folic acid deficiencies. Individuals without underlying hematological or neurological disorders may emerge with mental symptoms ⁽¹⁾.

Folate and vitamin B12 are essential for the carbon transfer metabolism required for serotonin synthesis, and this has been underlined by previous research between folic acid deficiencies with depressive disorders. Vitamin B12 and folic acid levels may be associated to neuropsychiatric disorders like OCD, according to some research. The severity of obsessive-compulsive disorder is inversely related to vitamin B12 deficiency, according to the available research.

This suggests that patients with OCD who are showing signs of resistance would benefit from taking vitamin B12 supplements. In addition, keeping an eye on your vitamin B12 levels is useful in OCD treatment ⁽²⁾.

The purpose of this study was to increase our understanding of how vitamin B12 and folic acid affect individuals with OCD so that we can better assess the severity of their symptoms and reduce their risk of death.

METHODS

From August 2022 to January 2023, researchers at Al-Azazy Hospital looked at the effectiveness of a review article on the hospital's addiction and mental health therapy. We filed for and received approval from the university's IRB (ZU-IRB #9456/10-4-2022). We collected and analyzed many studies that were relevant to our topic and wrote a narrative review of our findings.

The article:

Problems with obsessive compulsive disorder:

Obsessive-compulsive disorder (OCD) is characterized by repetitive, ritualized activities (compulsions) or persistent, distressing thoughts (obsessions) about a set of predetermined themes. For an extended amount of time, the person has no say over their thoughts or actions. Counting objects, checking locks multiple times, and repeatedly washing hands are all examples of common compulsions. Persistently engaging in these behaviors creates difficulties in one's day-to-day ⁽³⁾.

The root causes have yet to be identified. Identical twins are more likely to be affected than fraternal or fraternity-like twins, suggesting a familial link. Exposure to or experience with trauma as a child is one of the risk factors. Subsequent infections have been connected to several of the individuals. Using the patient's reported symptoms, a diagnosis is made, and then all other possible medical and drug-related reasons are ruled out. It is projected that 2.3% of the population will develop OCD throughout their lifetimes, and that 1.2% of the population will have the illness at any one

time. Problems typically manifest in those under the age of 20, and seldom in those above the age of 35. OCD affects roughly 4% as many males as women globally.

Relation of OCD with different vitamins:

Vitamin E: All of the tocopherols and tocotrienols that make up vitamin E are fat-soluble. Although vitamin E shortage is uncommon, when it does occur, it is often the result of a basic problem with the metabolism of dietary fat rather than a diet that is lacking in vitamin E. Despite this, vitamin E deficiency can still cause nerve problems. Cell membranes can be shielded from the damaging effects of oxidative stress by vitamin E, which is a fat-soluble antioxidant. A shortage in vitamin E is exceedingly unusual in humans and does not arise because there is a dearth of vitamin E in the food; rather, it occurs because of difficulties with fat absorption or metabolism. It's not uncommon for genes that code for proteins involved in metabolism to get mutated.

The alpha-tocopherol transfer protein (-TTP) is one example of this type of protein. Ataxia with vitamin E deficiency (AVED) is a progressive neurological condition that occurs in people who have this genetic mutation despite the patients having a normal diet that includes adequate levels of vitamin E. To compensate for the absence of -TTP, taking alpha-tocopherol as a dietary supplement in dosages that are sufficiently high is required. A deficit in vitamin E, which can be brought on by malabsorption or an imbalance in the metabolic process, can affect the shape and function of neuron membranes, which in turn can impair the normal conduction of electrical impulses along neurons. Ataxia is one of the many conditions that can be brought on by a deficiency in vitamin E, along with peripheral neuropathy, myopathies, blindness, and weakened immunological responses ^(5, 6). Individuals with OCD exhibited slightly lower plasma vitamin E concentrations than healthy persons ⁽⁷⁾, which may be related to the strong relationship among OCD and oxidative stress, which involves free radicals and the antioxidant defence. [Citation needed] Patients with OCD showed slightly lower plasma vitamin E concentrations than healthy persons ⁽⁷⁾.

Vitamin C: As an essential component of the diet of humans, vitamin C is an important nutrient. As an example, the synthesis of collagen and the healing of wounds are both enzymatic processes that require vitamin C as a cofactor. These processes are necessary for all animals, including humans. In humans, scurvy is more severe than in other animals because a shortage of vitamin C makes collagen creation more difficult ⁽⁸⁾. In addition to its various activities in biochemistry, vitamin C also functions as a reducing agent and an antioxidant. As an electron donor, it takes part in a wide variety of chemical reactions, both enzymatic and non-enzymatic. Vitamin C is oxidized during this process, which results in the production of either dehydroascorbic acid or semidehydroascorbic acid.

Enzymatic processes that are dependent on glutathione and NADPH are necessary for the conversion of these molecules back to their reduced form ⁽⁹⁾. Low levels of vitamin C have been linked to a variety of forms of cognitive impairment, including obsessive-compulsive disorder (OCD) and diseases such as Alzheimer's and dementia, according to the findings of multiple researchers. The Mini-Mental State Examination, which is essentially a generic test of cognition, was used for the cognitive testing. This demonstrates the typically low quality of studies evaluating the probable impact of vitamin C on cognition in healthy and impaired individuals ⁽⁷⁾.

Vitamin D: One of the many physiological effects of vitamin D is an increase in the intestinal absorption of calcium, magnesium, and phosphate. Vitamin D also has many other benefits. There have been reports of a variety of other biological consequences as well. Vitamin D3 (also known as cholecalciferol) and vitamin D2 (also known as ergocalciferol) are the two members of this class that are considered to be of the utmost significance in humans. The elderly, children, and adults of the world all have an alarmingly high prevalence of vitamin D insufficiency ⁽¹⁰⁾. A deficiency in vitamin D can induce a variety of bone diseases, including rickets in children and osteomalacia in adults. These diseases are characterized by improper bone mineralization and bone degradation. If you don't get enough sun exposure, your blood level of calcifediol, also known as 25-hydroxyvitamin D, may drop. It's possible that your body will only absorb 15% of the calcium that you consume if you don't get enough vitamin D. When a person is healthy, their rate of absorption falls somewhere between 60 and 80% ⁽¹⁰⁾. Numerous studies have demonstrated that there is a correlation between low levels of vitamin D at birth and the later emergence of mental and neurological conditions such as obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), cognition issues, and dementia. However, this correlation is only weak and does not prove causation. These individuals with psychiatric difficulties were improved by taking vitamin D supplements, according to the findings of a number of small randomized controlled trials ⁽⁷⁾.

Vitamin B6: Vitamin B6, which is classified as a B vitamin, is an essential nutrient. The term "vitamers" is an abbreviation for a group of six molecules that are chemically connected to one another and are capable of interacting with one another in living beings. These molecules are referred to as "vitamers." Its active form, known as pyridoxal 5'-phosphate, participates as a coenzyme in over 140 enzyme activities that are essential to the breakdown of lipids, carbohydrates, and amino acids ⁽¹¹⁾. There are many different parts of macronutrient metabolism that vitamin B6 is involved in. Some of these aspects include the production and

function of haemoglobin, synthesis of neurotransmitters and histamine, gene expression, and many others. Coenzymes, also known as cofactors, play an important role in many chemical reactions, including decarboxylation, transamination, racemization, elimination, replacement, and beta-group interconversion. Vitamin B6 plays this role frequently. It is necessary for the formation of serotonin, dopamine, adrenaline, norepinephrine, and gamma-aminobutyric acid (GABA), hence it is referred to as a cofactor⁽¹¹⁾. A seborrheic dermatitis-like eruption, atrophic glossitis with ulceration, angular cheilitis, conjunctivitis, intertrigo, neurologic symptoms of somnolence, confusion, and neuropathy (due to impaired sphingosine synthesis), as well as microcytic anemia (due to impaired heme synthesis), are all components of the classic clinical syndrome for vitamin B6 deficiency. Multiple studies have shown that individuals who suffer from OCD and cognitive impairment have significantly lower levels of vitamin B6 in their bodies^(7,8).

The dilemma of Vitamin B12 and folate in OCD (Figure 1):

The importance of folate and vitamin B12 in one's diet as a factor in the normal and aberrant operation of the neuropsychiatric system is being supported by an increasing body of research. According to the findings of certain studies, the percentage among individuals who exhibited neuropsychiatric symptoms ranged from 5% to 50% when they were deficient in vitamin B12. There has been a rise in the number of articles published in recent years that examine the possible therapeutic effects of folate and vitamin B12 in the treatment of mental illness⁽¹²⁾. Folate, vitamin B12, hereditary variables, and the metabolism of neurotransmitters all play a part in individuals who have obsessive-compulsive disorder (OCD). Researchers have attempted to demonstrate a connection between obsessive-compulsive disorder (OCD) and other psychiatric illnesses as their investigation of folate and its carbon unit metabolism has evolved. Nevertheless, they have discovered contradictory results⁽¹³⁾. Studies have been conducted to investigate the potential connections among OCD and blood levels of low folate, high homocysteine, or low vitamin B12, respectively. Individuals with OCD frequently have a desire for repetition, and the obsessions that afflict them cause them to experience sensations of anxiety, fear, and even revulsion. Because of this, OCD is typically accompanied by a number of other psychiatric diseases⁽⁷⁾.

It is generally accepted that the majority of children who suffer from OCD also have another axis I condition. It would appear that other anxiety disorders (with a prevalence rate of 50%) and depressive disorders (with a prevalence rate of 40%) have the highest rates of occurrence. OCD has been demonstrated to have a strong positive association with

high scores on the CDI depression scale and the STAI-2, which evaluates ongoing anxiety, by a number of writers. There has been researched on the levels of vitamin B12 and folic acid in OCD patients who are adults, however there were no research conducted on OCD children's patients or adolescents. Research suggesting that taking supplemental folate helps alleviate symptoms of depression lends credibility to the possibility that this nutrient has a role in psychopathology. Even though depression and anxiety disorders usually occur together, there hasn't been much research done on the influence of an altered one-carbon metabolism in anxiety disorders, particularly OCD. The lifetime prevalence of obsessive-compulsive disorder ranges from 1% to 3%, and it has a strong tendency to run in families⁽¹²⁾. As a consequence of this, it lowers the quality of life for those being treated as well as the people who care about them. It may be beneficial to research the roles of vitamin B12, folate, and homocysteine given the impact that OCD has on the quality of life of patients as well as the quality of life of their families and the potential that it has to supplement medication in a different way⁽⁷⁾.

Multiple research that investigated this topic came to the conclusion that patients had significantly lower levels of folic acid and vitamin B12 compared to the healthy controls in the investigations. Folic acid deficiencies are common in individuals who suffer from OCD⁽¹⁴⁾. OCD patients were shown to have low amounts of vitamin B12, elevated levels of homocysteine, and undetectable levels of folic acid, according to **Turksoy et al.**⁽¹³⁾. According to the findings of other studies, a lack of vitamin B12 may also be associated with the symptoms of OCD. When taken together, these data raise the possibility that components of the metabolism of one carbon, such as homocysteine, folic acid, and vitamin B12, may play a part in the development of obsessive-compulsive disorder. In addition to being necessary for the production of DNA, the one-carbon metabolism is also required for the methylation of proteins, neurotransmitters, and phospholipids in the brain membrane. Some neuropsychiatric disorders may have their roots in metabolic pathways, which are frequently neglected in medical research. Inadequate amounts of folic acid and vitamin B12 are the root cause of low levels of neurotransmitters, which may be traced back to deficits in methylation processes, which are in turn caused by a lack of folic acid⁽⁷⁾. It is also possible for there to be an increase in dangerously high levels of homocysteine. When homocysteine levels are too high, there is a risk of experiencing DNA damage, stress on the endoplasmic reticulum, and dysfunction in the mitochondria. They accomplish this by activating NMDA receptors, which in turn results in an increase in calcium entry into cells. Heightened levels of oxidative stress within the cell as well as activation of apoptotic signaling⁽¹²⁾.

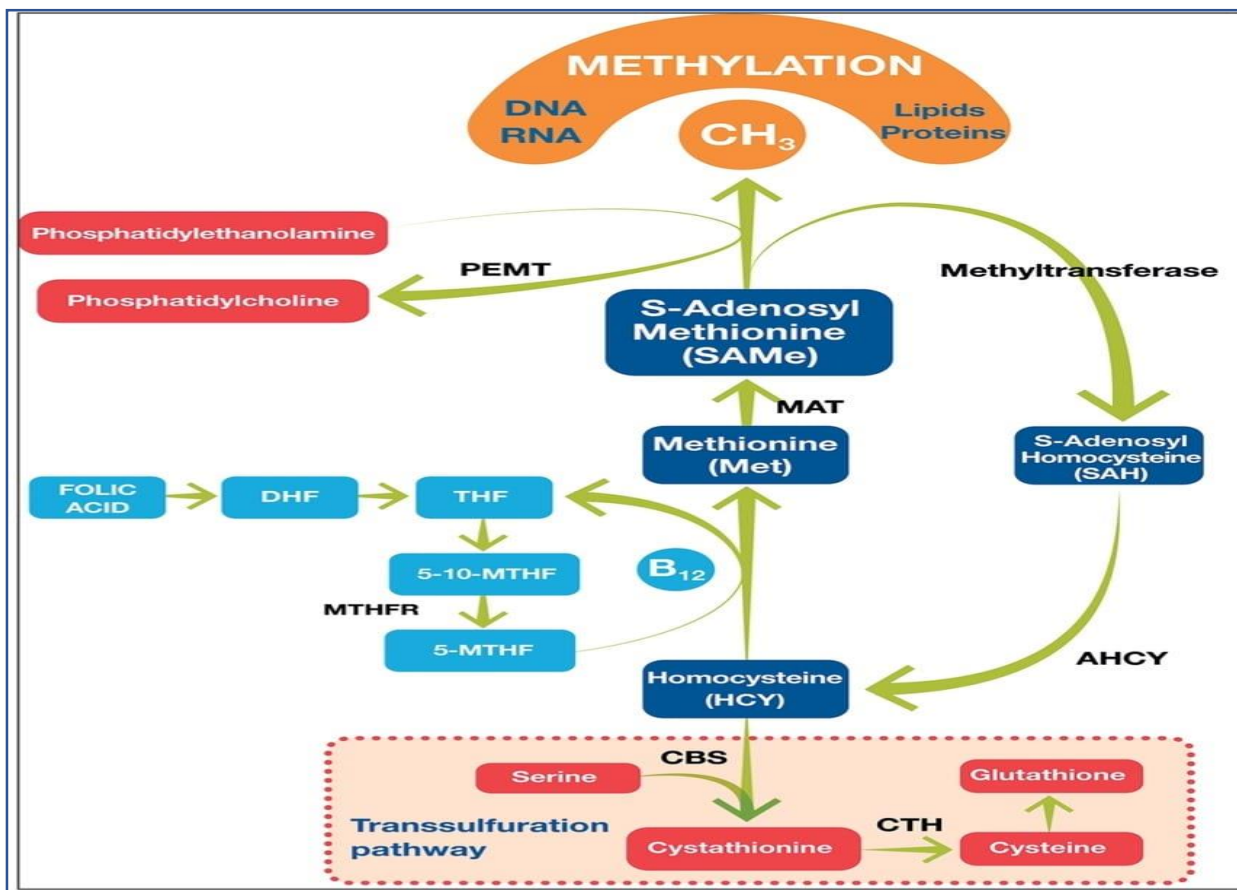


Figure (1): Folic acid and vitamin B12 provide a synergistic effect in the treatment of psychiatric disorders ⁽¹⁵⁾

Special considerations associated with COVID-19:

The therapeutic difficulties of treating psychiatric diseases like OCD are widespread. The occurrence of these problems has increased over the previous decade, particularly in the present era of the COVID-19 epidemic. Symptom management is complicated by these diseases due to their heterogeneous origins ⁽¹⁶⁾. Because standard antidepressant treatment overlooks potential contributors such as dietary inadequacies, oxidative stress, inflammation, neuroprotection, and neurogenesis. It may not be effective for all patients with OCD. Patients with OCD who do not show improvement with normal treatment have even fewer options. The new discipline of nutritional psychiatry seeks to pinpoint which nutrients are crucial for mental well-being. Patients who do not improve while on antidepressants or mood stabilizers may benefit from a number of complementary treatments, such as recommending dietary adjustment or supplementation with medicinal foods and supplements to address dietary imbalances ⁽⁷⁾.

Numerous studies, though not all, have found that adding folic acid and vitamin B12 to one's diet can help reduce the signs and symptoms of depression and other mood disorders. Depending on the severity of the illness, vitamin B12 and folic acid supplements may be required; for mild to moderate symptoms and difficulties on the verge of diagnosis, oral

supplementation alone may suffice ⁽¹²⁾. Depression that is mild or short-lived may also benefit from this approach. Subthreshold depression, seasonal mood disorders, anxious-depressive syndromes, and diseases related to the COVID-19 pandemic may benefit from folic acid and vitamin B12 supplementation as first-line therapy. There is evidence that the COVID-19 pandemic is responsible for a variety of interrelated mental problems, such as insomnia, depression, and post-traumatic stress disorder ⁽¹⁵⁾.

Additionally, to curing symptoms with minimal to no negative side effects, the initial supplementary treatment may aid subsequent pharmaceutical therapy in the event of worsening symptoms. From what we've seen in the lab ⁽¹⁷⁾, these medicines appear to have a good safety profile. Symptoms like irritation, stress, and fatigue may be alleviated by making immediate and significant changes to one's diet or by taking vitamin B12 and folic acid pills. As a result, the efficacy of conventional pharmaceutical treatment may improve over time. This is because of the compounds' efficacy, useful clinical results, and lack of toxicity. When making treatment decisions for mental and psychological problems, the relative efficacy and safety of various drugs may be taken into account ^(7, 8). Orodispersible combinations are useful when time and efficacy are of the essence. Increased bioavailability and a quicker beginning of action may result from the

orodispersible formulation's potential for rapid absorption into the bloodstream. There is a need for additional clinical trials to corroborate the findings and examine the full scope of benefits and negatives of these drugs because of methodological difficulties⁽¹⁵⁾ and the inconsistency of the research evaluated here.

CONCLUSION AND RECOMMENDATIONS

We come to the conclusion that OCD is one of the most frequent mental illnesses and that a proper diagnosis should be the doctor's main focus when treating these cases from the start to prevent potentially harmful sequences and to better understand the causes and treatments of OCD. Low levels of vitamin B12 and folic acid were also associated with neuropsychiatric diseases such as OCD that we investigated. Lack of B12 and folic acid has also been linked to psychiatric symptoms and impairments in brain function. We urge that doctors keep an eye out for individuals with OCD who have high serum levels of vitamin B12 and folic acid until more thorough and high-quality studies can be conducted. Our findings can serve as a starting point for future research in this area.

DECLARATIONS

- **Consent for publication:** All authors agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
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- **Conflicts of interest:** No conflicts of interest.

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