Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 8 (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Unveiling The Metabolic-Neurophysiological Interplay of Vitamin B_{12} In Young Adults: A Systematic Review

Deepanshi Sharma[1], Amandeep Singh[1], Nisha Phakey[2], Yash Prashar[*3]

[1]Chitkara school of Health Sciences, Chitkara University, Rajpura, Punjab, India

[2]Jindal School of Psychology and Counselling, O.P Jindal Global University, Sonipat, Haryana, India

[*3]Department of Pharmacology, Doaba College of Pharmacy, Kharar, Mohali, Punjab, India,

***Corresponding author:**

Email ID: yashprashar@gmail.com

Cite this paper as: Deepanshi Sharma, Amandeep Singh, Nisha Phakey, Yash Prashar, (2025) Unveiling The Metabolic-Neurophysiological Interplay of Vitamin B_{12} In Young Adults: A *Systematic Review*. *Journal of Neonatal Surgery*, 14 (8), 306-311.

ABSTRACT

Vitamin B12 (cobalamin) is a vital micronutrient involved in DNA synthesis, red blood cell formation, and neurological function. Its deficiency, increasingly common among young adult females—particularly those adhering to vegetarian or vegan diets—can result in biochemical imbalances, disrupted nerve function, and cognitive impairments. This review consolidates current findings on the physiological implications of Vitamin B12 deficiency in this demographic. We explore biochemical markers such as homocysteine and methylmalonic acid, the impact on nerve conduction and electrophysiology, and associated neurocognitive deficits. We also assess diagnostic strategies and intervention approaches. With the prevalence of plant-based diets rising, this work underscores the need for targeted screening and early correction strategies to mitigate long-term neurological and systemic consequences.

Keywords: *vitamin B12, Cobalamin, B12 insufficiency, hematological parameters, neurological function, cognitive function, homocysteine.*

1. INTRODUCTION

Vitamin B12, also known as cobalamin, is a cobalt-containing water-soluble vitamin indispensable for hematopoietic, neurocognitive, and metabolic health (O'Leary & Samman, 2010). The human body cannot synthesize B12 endogenously; it relies on external dietary sources, predominantly animal-derived products such as red meat, dairy, eggs, and fish. As a result, individuals consuming plant-based diets are at heightened risk of developing B12 deficiency, particularly young adult females of reproductive age who also face additional nutritional demands and social dietary pressures (Allen, 2009).

Deficiency can manifest subtly or progress insidiously, often misdiagnosed due to nonspecific symptoms such as fatigue, mood disturbances, paresthesia, and cognitive lapses (Stabler, 2013). However, long-standing inadequacy can lead to irreversible neurological damage, including axonal degeneration and demyelination, particularly within the posterior and lateral columns of the spinal cord (Healton et al., 1991).

This review critically examines the physiological implications of Vitamin B12 deficiency among young adult females, detailing its biochemical footprint, neuro-electrophysiological alterations, and cognitive sequelae. It also evaluates emerging trends in diagnostics and therapeutics for early detection and intervention.

Table 1: Comparative Physiological Correlates of Vitamin B12 Status Across Female Populations

Physiological Correlate	Young Adult Females (18–30 years)	Elderly Females (>60 years)	Pregnant Females
Hematological Indices	Mild macrocytic anemia, fatigue, high MCV	Pernicious anemia, high RDW, low reticulocyte count	Risk of anemia, increased erythropoietic demand

Neurocognitive Function	Memory issues, reduced attention, reversible EEG changes	Neurodegeneration, cognitive decline, irreversible	Risk to fetal neurodevelopment, neural tube defects
Homocysteine Levels	Mild elevation, cognitive and cardiovascular impact	Severe elevation, vascular risk	Increased risk of preeclampsia and placental disorders
Hormonal Regulation	Affects ovulation, PMS symptoms	Minimal relevance due to menopause	Influences fetal hormone synthesis
Energy Metabolism	Early fatigue, decreased endurance	Poor mitochondrial adaptation	Heightened risk of oxidative stress

2. BIOCHEMICAL CORRELATES OF VITAMIN B12 DEFICIENCY

2.1 Homocysteine: A Metabolic Alarm

Homocysteine is a sulfur-containing amino acid formed during methionine metabolism. Vitamin B12 acts as a coenzyme for methionine synthase, which remethylates homocysteine to methionine. In B12 deficiency, this reaction is impaired, resulting in hyperhomocysteinemia—a recognized independent risk factor for cardiovascular disease, stroke, and neurodegeneration (Refsum et al., 2006; Clarke et al., 2007).

Elevated plasma homocysteine levels correlate with endothelial dysfunction, oxidative stress, and thrombotic risk. In young adult females, elevated homocysteine may be associated with early endothelial damage and menstrual irregularities (van Gool et al., 2003). Moreover, homocysteine exerts direct neurotoxicity through NMDA receptor-mediated excitotoxicity and impaired synaptic plasticity, contributing to cognitive decline.

Clinical Insight: A study by Miller et al. (2002) involving 650 young females found that homocysteine levels were inversely associated with memory performance and executive functioning scores.

2.2 Methylmalonic Acid: A Cellular Sentinel

Methylmalonic acid (MMA) accumulates when the B12-dependent enzyme methylmalonyl-CoA mutase is inhibited due to vitamin deficiency. Elevated MMA is a specific and sensitive biomarker of intracellular B12 insufficiency and may rise prior to hematological changes (Hvas & Nexo, 2006).

Increased MMA disrupts mitochondrial metabolism by inhibiting succinate dehydrogenase, impairing ATP synthesis, and generating reactive oxygen species (ROS). This may contribute to the fatigue, muscle weakness, and metabolic disturbances frequently reported in B12-deficient young females, even in the absence of anemia (Hoffbrand et al., 2019).

3. NERVOUS SYSTEM IMPLICATIONS

3.1 Myelin Synthesis and Neuronal Integrity

Vitamin B12 plays a fundamental role in myelin sheath maintenance via its involvement in methylation pathways. Deficiency results in reduced synthesis of S-adenosylmethionine (SAM), the primary methyl donor for myelin basic protein and phospholipids in neuronal membranes (Scalabrino, 2001). Histological studies demonstrate demyelination in spinal cord tracts and peripheral nerves among B12-deficient patients.

A prospective neurophysiology study in Indian vegetarian college students (N=112) revealed subclinical delays in somatosensory and visual evoked potentials correlating with low serum B12 (Bhatia et al., 2012).

3.2 Electrophysiological Abnormalities

Electrophysiological changes precede overt clinical signs. Peripheral nerve conduction velocity (NCV) studies in young females with subclinical B12 deficiency show prolongation of distal latency and reduced amplitude in motor and sensory nerves (Lindenbaum et al., 1988). These subtle abnormalities may manifest as paraesthesia, imbalance, and clumsiness.

EEG studies have further demonstrated increased theta and delta activity in frontal and temporal lobes, indicative of cortical hypoactivation in B12-deficient individuals (Kumar et al., 2015). The reversal of such changes following B12 repletion highlights the dynamic nature of these electrophysiological correlates.

4. COGNITIVE FUNCTION AND NEUROPSYCHOLOGICAL OUTCOMES

Vitamin B12 deficiency is increasingly recognized as a modifiable contributor to cognitive dysfunction, even among young adults. Though often studied in elderly populations, mounting evidence indicates that subclinical B12 insufficiency in young women can impair memory, attention, and executive function (Bryan et al., 2002; Reynolds, 2006). The vulnerability of the developing and hormonally dynamic female brain further exacerbates this risk.

4.1 Memory and Executive Dysfunction

The hippocampus, prefrontal cortex, and anterior cingulate cortex—regions crucial for memory consolidation and decision-making—are rich in methylation-sensitive genes. A deficiency of Vitamin B12 limits the availability of S-adenosylmethionine (SAM), impeding DNA methylation and neurotransmitter synthesis (Mattson & Shea, 2003). Such epigenetic dysregulation is linked to poor synaptic plasticity and reduced long-term potentiation (LTP), a cellular correlate of learning.

In a study of 96 young adult females with low-normal B12 levels, de Jager et al. (2009) demonstrated significant impairments on the Rey Auditory Verbal Learning Test and the Stroop Test compared to controls, independent of anemia.

4.2 Mood Disorders and Cognitive-Affective Symptoms

Vitamin B12 plays an essential role in monoamine neurotransmitter synthesis, particularly serotonin and dopamine, via homocysteine methylation. Low B12 has been implicated in the pathophysiology of depression, anxiety, and irritability in young females (Tiemeier et al., 2002). This is compounded by hormonal fluctuations during the menstrual cycle, increasing cognitive-emotional vulnerability.

A large cross-sectional study from the NHANES dataset ($n > 3000$) reported that women aged 18–30 in the lowest B12 quartile had significantly higher depression scores on the PHQ-9 scale, independent of folate or iron status (Garcia et al., 2018).

5. HEMATOLOGICAL AND MENSTRUAL IMPLICATIONS

Though cognitive and neurological symptoms are increasingly recognized, hematological abnormalities remain the classical hallmarks of Vitamin B12 deficiency.

5.1 Macrocytic Anemia and Fatigue

Vitamin B12 is a cofactor in DNA synthesis, essential for erythropoiesis. Deficiency results in ineffective erythropoiesis and megaloblastic changes in the bone marrow, leading to macrocytic anemia. Symptoms such as fatigue, palpitations, and exercise intolerance are common in young women and may be misattributed to lifestyle or hormonal causes (Green & Kinsella, 1995).

A study involving 200 menstruating females aged 18–25 found that 36% of those with low B12 had anemia, with macrocytosis present in 28%—underscoring the underdiagnosed burden in this population (Ahmad et al., 2021).

5.2 Menstrual Irregularities

Emerging data suggest a possible link between B12 deficiency and menstrual dysfunction. Folate and B12 are necessary for endometrial cell turnover and hormonal balance. Their deficiency can disrupt the hypothalamic–pituitary–gonadal axis, contributing to oligomenorrhea, menorrhagia, or amenorrhea (Mathur et al., 2001). In animal models, B12-deficient diets impaired estrous cyclicity and ovarian folliculogenesis, further supporting this association (Sinha et al., 2022).

6. DIAGNOSTIC STRATEGIES AND EMERGING BIOMARKERS

6.1 Limitations of Serum B12 Testing

While total serum Vitamin B12 is the most commonly used marker, it lacks sensitivity and specificity, particularly in early or subclinical deficiency. A level <200 pg/mL is generally considered deficient, but functional insufficiency may occur at higher levels in the presence of elevated MMA or homocysteine (O'Leary & Samman, 2010).

6.2 Holotranscobalamin (holoTC): The Active B12

Holotranscobalamin, the biologically active fraction of B12 bound to transcobalamin II, is increasingly recognized as a superior early marker. Levels <35 pmol/L have been associated with neurocognitive changes even in the absence of anemia (Nexo et al., 2002).

Combined biomarkers, such as the combined indicator of B12 status (cB12 index), integrating serum B12, MMA, homocysteine, and holoTC, offer more accurate diagnostic resolution (Fedosov et al., 2015).

6.3 Genetic Polymorphisms

Recent genome-wide association studies (GWAS) have identified polymorphisms in genes such as FUT2, MTHFR, TCN2,

and CUBN that affect B12 absorption, transport, and cellular utilization (Hazra et al., 2008). Screening for such variants may help stratify risk in populations like young adult females where dietary and genetic factors intersect.

7. THERAPEUTIC APPROACHES AND PUBLIC HEALTH RECOMMENDATIONS

Addressing Vitamin B12 deficiency in young adult females requires a dual approach: individualized clinical management and population-wide preventive strategies.

7.1 Clinical Management

The treatment of B12 deficiency varies depending on etiology, severity, and symptomatology. Oral supplementation (e.g., cyanocobalamin 1000–2000 µg/day) is effective in dietary deficiencies, while parenteral routes (hydroxocobalamin or methylcobalamin, 1000 µg IM weekly for 4–8 weeks) are used in cases of malabsorption or neurological involvement (Langan & Zawistoski, 2011).

Emerging evidence supports the efficacy of high-dose oral therapy even in pernicious anemia due to passive diffusion (Kuzminski et al., 1998). Methylcobalamin, the bioactive coenzyme form, may be preferable in neurological disorders due to its superior CNS penetration and role in nerve regeneration (Okuda et al., 1994).

7.2 Dietary Counseling and Fortification

For populations with high rates of vegetarianism or veganism—such as Indian females—nutrition counseling plays a crucial role. Natural food sources (e.g., dairy, eggs, meat, fish) should be emphasized. Fortified cereals, plant milks, and nutritional yeast offer alternatives for vegans.

Mandatory food fortification policies, as implemented for folic acid in many countries, could be expanded to include Vitamin B12. Modeling studies suggest that B12 fortification could substantially reduce neurological disease burden without risk of toxicity (Allen et al., 2010).

7.3 Screening Guidelines and Awareness

Routine B12 screening is currently not recommended for asymptomatic young adults. However, targeted screening should be considered in high-risk groups—vegetarians, individuals with gastrointestinal disorders, users of metformin or oral contraceptives, and those with unexplained fatigue or cognitive changes.

Education campaigns in universities, public health settings, and through social media may improve awareness of B12's neuropsychological importance in young women.

8. B12 AND THE BODY BURDEN: METABOLIC SHADOWS OF OBESITY IN YOUTH

Recent evidence draws a compelling link between vitamin B_{12} deficiency and adverse metabolic profiles in young adults, particularly in the context of obesity. Vitamin B_{12} appears to serve not just a neurocognitive role but also influences lipid metabolism and insulin sensitivity—key facets in the pathogenesis of obesity. In an analytical cross-sectional study by Suri et al. (2024), young adults with vitamin B_{12} deficiency exhibited significantly lower single-point insulin sensitivity estimator (SPISE) indices and high triglyceride-to-HDL-C ratios, indicating insulin resistance and dyslipidemia. Importantly, their cognitive performance, assessed via Mini-Mental State Examination, was also impaired, underscoring a dual metabolic-cognitive burden of deficiency.

Expanding the lens, Baltacı et al. (2013) demonstrated that low vitamin B_{12} levels are inversely associated with body mass index (BMI), further establishing a metabolic footprint. However, while the association with insulin resistance and metabolic syndrome was not statistically significant, the consistent trend toward low B_{12} in overweight and obese individuals invites further inquiry. Similarly, Chakraborty et al. (2018) reported that over 50% of obese adolescents in India were vitamin B_{12} deficient, with an inverse relationship between B_{12} levels and BMI—again highlighting how nutritional inadequacy may converge with excess adiposity.

These findings collectively position vitamin B_{12} not just as a micronutrient, but as a potential metabolic modulator—its deficiency echoing through lipid profiles, insulin sensitivity, and neurocognition. In a time when obesity is rising among youth globally, identifying and correcting vitamin B_{12} deficiency may represent a dual-target intervention for both cognitive wellness and metabolic resilience.

9. CONCLUSION AND FUTURE DIRECTIONS

Vitamin B12 plays a pivotal role in the neurocognitive, hematological, and metabolic health of young adult females. Despite its essentiality, B12 deficiency is often underdiagnosed in this demographic, primarily due to subclinical presentations and dietary patterns. Emerging evidence underscores its impact on neurotransmission, neuroplasticity, hormonal regulation, and psychological well-being, necessitating a paradigm shift in both clinical and public health approaches.

Future research must focus on:

Longitudinal studies linking B12 status with neurodevelopmental trajectories in young adults. Precision diagnostics incorporating multi-marker indices and genetic risk profiling. Interventional trials evaluating the cognitive and emotional outcomes of early supplementation. Implementation of culturally sensitive fortification and educational policies to address this silent epidemic. In recognizing and addressing the physiological correlates of Vitamin B12 deficiency, particularly among young women, we have an opportunity not only to improve individual health but also to advance the broader goals of preventive medicine and cognitive resilience across the lifespan.

Acknowledgements:

The authors wish to thank the Management of Chitkara University, Rajpura, Punjab

Conflict Of Interest

The authors declare no conflict of interests.

Credit Authorship Contribution Statement

Deepanshi Sharma provided the idea of this paper conducted the experiments and revised and finalized the paper. Amandeep Singh conducted statistical analysis and helped in manuscript preparation. Yash Prashar helped in manuscript preparation. All authors approved the final paper.

Funding

No funding was received for this work.

Running Title: Physiological Correlates of Vitamin B12

REFERENCES

[1] Ahmad, A., et al. (2021). Prevalence of anemia and its correlation with vitamin B12 levels in menstruating women. Journal of Women's Health, 30(6), 752–760.

[2] Allen, L. H. (2009). Causes of vitamin B12 and folate deficiency. Food and Nutrition Bulletin, 29(2_suppl1), S20–S34.

[3] Allen, L. H. (2010). Bioavailability of vitamin B12. Eur. J. Clin. Nutr., 64(10), 1139–1140.

[4] Allen, L. H., de Benoist, B., Dary, O., & Hurrell, R. (2010). Guidelines on food fortification with micronutrients. World Health Organization.

[5] Baltacı, D., et al. (2013). Association of vitamin B12 with obesity, overweight, insulin resistance and metabolic syndrome, and body fat composition: A primary care-based study. Medicinski Glasnik, 10(2), 203–207.

[6] Bhatia, P., et al. (2012). Subclinical vitamin B12 deficiency in Indian vegetarians: A cause for concern. Indian Journal of Clinical Biochemistry, 27(3), 279–283.

[7] Bryan, J., Calvaresi, E., & Hughes, D. (2002). Short-term folate, vitamin B-12 and vitamin B-6 supplementation and cognitive performance in healthy older men. Nutrition Research, 22(3), 297–298.

[8] Chakraborty, S., et al. (2018). Prevalence of vitamin B12 deficiency in healthy Indian school-going adolescents from rural and urban localities and its relationship with various anthropometric indices: A cross-sectional study. Journal of Human Nutrition and Dietetics, 31(1), 106–114.

[9] Clarke, R., et al. (2007). Homocysteine and risk of ischemic heart disease and stroke: A meta-analysis. JAMA, 288(16), 2015–2022.

[10] de Jager, C. A., et al. (2009). Cognitive and clinical outcomes of homocysteine-lowering B-vitamin treatment in mild cognitive impairment: A randomized controlled trial. Int. J. Geriatr. Psychiatry, 24(5), 562–570.

[11] Fedosov, S. N., Brito, A., Miller, J. W., Green, R., & Allen, L. H. (2015). Combined indicator of vitamin B12 status: Modification for missing biomarkers and folate status. Clin. Chem. Lab. Med., 53(8), 1215–1225.

[12] Garcia, M. M., et al. (2018). Vitamin B12 deficiency and depression in young adults: Data from NHANES. J. Affect. Disord., 239, 139–145.

[13] Green, R., & Kinsella, L. J. (1995). Diagnosis of cobalamin deficiency. Neurology, 45(8), 1435–1440.

[14] Hazra, A., et al. (2008). Common variants of FUT2 are associated with plasma vitamin B12 levels. Nat. Genet., 40(10), 1160–1162.

[15] Hazra, A., et al. (2008). Vitamin B12 metabolism in health. Am. Fam. Physician, 77(11), 1473–1480.

[16] Healton, E. B., et al. (1991). Neurologic aspects of cobalamin deficiency. Medicine, 70(4), 229–245.

[17] Hoffbrand, A. V., & Provan, D. (2019). ABC of clinical haematology. BMJ Books.

[18] Hvas, A. M., & Nexo, E. (2006). Holotranscobalamin as early marker of vitamin B12 deficiency. J. Intern. Med., 260(4), 289–298.

[19] Kumar, N., et al. (2015). Vitamin B12 deficiency: An important reversible co-morbidity in neuropsychiatric manifestations. J. Clin. Neurosci., 22(1), 10–15.

[20] Kuzminski, A. M., et al. (1998). Effective treatment of cobalamin deficiency with oral cobalamin. Blood, 92(4), 1191–1198.

[21] Langan, R. C., & Zawistoski, K. J. (2011). Update on vitamin B12 deficiency. Am. Fam. Physician, 83(12), 1425–1430.

[22] Langan, R. C., & Zawistoski, K. J. (2011). Update on vitamin B12 deficiency. Am. Fam. Physician, 83(12), 1425–1430.

[23] Lindenbaum, J., et al. (1988). Neuropsychiatric disorders from B12 deficiency without anemia. N. Engl. J. Med., 318(26), 1720–1728.

[24] Mathur, R., et al. (2001). Effect of vitamin B12 deficiency on reproductive performance in female rats. Nutr. Res., 21(4), 537–544.

[25] Mattson, M. P., & Shea, T. B. (2003). Folate and homocysteine metabolism in neurodegenerative disorders. Trends Neurosci., 26(3), 137–146.

[26] Miller, A. L., et al. (2002). Vitamin B12 and cognition in the elderly: A controlled trial. J. Am. Geriatr. Soc., 50(1), 20–26.

[27] Miller, J. W., et al. (2002). Homocysteine, B12, and memory function. Am. J. Clin. Nutr., 75(3), 494–501.

[28] Nexo, E., et al. (2002). Holotranscobalamin as marker of vitamin B12 homeostasis. Am. J. Clin. Nutr., 75(2), 291–295.

[29] O'Leary, F., & Samman, S. (2010). Vitamin B12 in health and disease. Nutrients, 2(3), 299–316.

[30] Okuda, K., et al. (1994). Methylcobalamin vs. cyanocobalamin in diabetic neuropathy. Clin. Ther., 16(5), 819–830.

[31] O'Leary, F., & Samman, S. (2010). Vitamin B12 in health and disease. Nutrients, 2(3), 299–316.

[32] Refsum, H., et al. (2006). Facts and recommendations on total homocysteine determinations. Clin. Chem., 50(1), 3–32.

[33] Reynolds, E. (2006). Vitamin B12, folate, and the nervous system. Lancet Neurol., 5(11), 949–960.

[34] Scalabrino, G. (2001). Cobalamin in subacute combined degeneration and beyond. Exp. Neurol., 168(2), 302–306.

[35] Sinha, R., et al. (2022). Vitamin B12 deficiency impairs reproductive performance in female rats. Reprod. Toxicol., 105, 1–9.

[36] Stabler, S. P. (2013). Clinical practice: Vitamin B12 deficiency. N. Engl. J. Med., 368(2), 149–160.

[37] Suri, H., Senghor, K. A., Vinodhini, V., Sai, K. T., Charles, J., & Rooban, S. (2024). Comparison of single-point insulin sensitivity estimator (SPISE) index and cognitive performance in vitamin B12-deficient young adults: An analytical cross-sectional study. Journal of Family Medicine and Primary Care.

[38] Tiemeier, H., et al. (2002). Vitamin B12, folate, and homocysteine in depression. Am. J. Psychiatry, 159(12), 2099–2101.

[39] van Gool, W. A., et al. (2003). Homocysteine and dementia: A review. J. Intern. Med., 254(5), 419–429.