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The Importance Of Vitamin B12 For Cardiovascular Patients

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Abstract:
Background*: Cardiovascular disease remains the leading cause of death globally, and nutritional interventions represent a modifiable factor with great therapeutic potential, as vitamin B12 plays an essential role in cardiovascular health through multiple interconnected mechanisms. Studies show that vitamin B12 deficiency is common among cardiovascular patients*
Materials and Methods*: This comprehensive article, based on a narrative review methodology and compiling evidence from the literature such as epidemiological studies, randomized controlled trials, and meta-analyses, aims to clarify the role of vitamin B12 (cobalamin) in cardiovascular health, particularly its role in homocysteine metabolism.*
Results*: Hyperhomocysteinemia, resulting from vitamin B12 deficiency, has been shown to be a risk factor for atherosclerosis, as its mechanism of action includes endothelial cell damage, increased oxidative stress, and enhanced inflammation Increased clotting predisposition. Analyses indicate that low vitamin B12 intake is independently associated with an increased risk of cardiovascular disease. Supplements targeting specific populations with hyperhomocysteineemia have significantly improved metabolic parameters and decreased the frequency of thrombotic events. Furthermore, individualized approaches that take into account genetic, demographic, and clinical factors when managing vitamin B12 deficiency yield beneficial therapeutic outcomes.*
Conclusion: *Routine assessment of vitamin B12 status should be performed for cardiovascular patients, by monitoring serum B12 levels, homocysteine concentrations, and lipid profiles with a particular focus on high-risk groups.*
Key Word: *Vitamin B12, heart disease, homocysteine, hyperhomocysteinemia, atherosclerosis*
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I. Introduction

Vitamin B12 (cobalamin) is a water-soluble vitamin essential for many biological processes including cellular energy production, methylation, and DNA synthesis. A deficiency of this vitamin can harm blood, cardiovascular, and nervous system health, especially in populations at risk due to dietary habits, age, genetic predisposition, or comorbidities. For cardiovascular patients, understanding the roles and clinical significance of vitamin B12 is critical to overall health care.

The biochemical role and pathophysiology of cardiovascular diseases

Vitamin B12 works in coordination with folic acid and vitamin B6 in the monocarbon metabolic cycle, which is essential for DNA synthesis and methyl reactions. Its most notable cardiovascular importance comes from its role in homocysteine metabolism: it acts as a cofactor for methionine synthase, facilitating the remethylation of homocysteine to methionine. The deficiency leads to hyperhomocysteineemia, a recognized — albeit mechanically debated— risk factor for atherosclerosis and thus cardiovascular disease (CVD) [1].

Hyperhomocysteinemia contributes to endothelial dysfunction and vascular damage. Clinical and experimental evidence confirms its association with an increased risk of coronary artery disease, stroke, and other atherothrombotic events, as well as microvascular complications [2]. Routine supplementation with B vitamins, including B12, effectively reduces homocysteine levels and shows beneficial effects on vascular health, especially in prevention strategies [3].

Biochemistry, metabolism, and deficiency mechanisms

Vitamin B12 acts primarily as a cofactor in two main enzyme reactions:

- Methionine synthase: converts homocysteine to methionine, and binds the B12 state to homocysteine metabolism and methylation pathways.
- Methylmalonyl-Co-A mutase: Converts methylmalonyl-Co to succinyl-Co, and involves mitochondrial metabolism and energy production.
- Causes of vitamin B12 deficiency:
- Food shortages (especially among people on a strict vegetarian diet)

- Gastrointestinal disease-causing impaired absorption (post-gastric surgery, pernicious anemia, ileal disease, atrophic gastritis)
- Medications (the most important of which is the use of metformin in diabetes)
- A genetic disorder affecting endogenous factor, transcobalamin, or B12 metabolism enzymes

Vitamin B12 deficiency leads to the accumulation of homocysteine and methylmalonic acid, each of the latter two compounds being associated with vascular dysfunction, anemia, and neurotoxicity [1].

Prevalence of vitamin B12 deficiency in cardiovascular patients

Vitamin B12 deficiency is widespread, especially among older adults and individuals with food restriction or malabsorption syndromes. Its deficiency is particularly prevalent among diabetics, those with metabolic syndrome, and chronic kidney disease—, that is, patient groups disproportionately affected by cardiovascular disease .[4].

Epidemiological studies indicate an important inverse relationship between levels. Serum vitamin B12 and key cardiovascular/metabolic indicators, including fasting blood sugar, and insulin resistance in postmenopausal women [5].

Furthermore, research in patients with type 2 diabetes reveals that treatment with metformin —the mainstay of glucose control— can induce or exacerbate vitamin B12 deficiency, increasing the risk of cardiovascular disease by increasing homocysteine and impairing lipid metabolism [6].

Vitamin B12, homocysteine, and atherosclerosis

Elevated plasma homocysteine, known as hyperhomocysteinemia, is a known risk factor for vascular disease. Homocysteine causes damage to endothelial cells, increases oxidative stress, and in addition, it promotes inflammation and enhances clotting effectiveness [2]. Homocysteine-lowering treatments using vitamin B12, vitamin B6, and folic acid can effectively reduce homocysteine levels. However, large trials have provided mixed results for reducing clinical endpoints in cardiovascular disease—most likely due to patient selection, background therapy, baseline levels, and genetic heterogeneity [3].

Outcomes for B12, homocysteine, and cardiovascular disease

Meta-analyses of clinical trials suggest that low vitamin B12 intake (along with folic acid and vitamin B6) is independently associated with a higher risk of cardiovascular disease [3]. While some large randomized trials have not shown a strong clinical benefit of homocysteine-lowering therapy in reducing major adverse cardiovascular outcomes, there is strong evidence to support the correction of moderate to severe hyperhomocysteine in mitigating the recurrence of vascular events, especially when deficiencies are identified and corrected [7]. This applies to patients with genetic or acquired disorders of one-carbon metabolism or chronic kidney failure, in which hyperhomocysteinemia is common [8].

Lipids Metabolism and Cardiac Effects

The role of vitamin B12' extends beyond homocysteine regulation. Emerging studies highlight its impact on lipid metabolism - a key risk factor for cardiovascular disease - by influencing epigenetic mechanisms such as DNA methylation, histone modifications, and RNA microexpression. Vitamin B12 deficiency has been linked to harmful lipid levels, including high triglycerides and unfavorable HDL cholesterol/high-density lipoprotein ratios, especially in patients with type 2 diabetes [9] .These changes may contribute to an increased risk of atherosclerosis [6].

Vitamin B12, fat metabolism and glucose

Emerging research links vitamin B12 deficiency to dysregulation of lipid metabolism, possibly through epigenetic mechanisms (DNA methylation and histone modifications) that affect genes associated with lipid and glucose homeostasis [4]. In diabetics, especially those taking metformin, low B12 levels are associated with high triglycerides and harmful cholesterol levels, increasing the risk of cardiovascular disease [5].

Population and gender considerations

There are marked differences in vitamin B12 metabolism and cardiovascular effects by sex, age, and genetic polymorphisms. Women, especially after menopause, are at increased risk of metabolic complications associated with vitamin B12 deficiency. Designing nutritional supplementation strategies based on these factors may improve cardiometabolic outcomes and should be considered in clinical recommendations [10].

Older adults are at increased risk of vitamin B12 deficiency due to decreased gastric acid secretion and altered absorption [6]. Women, especially postmenopausal women, may experience higher rates of deficiency and associated metabolic syndrome features such as increased insulin resistance and a higher risk of cardiovascular disease [7].

There are sex-specific differences in vitamin B12 metabolism and cardiovascular disease risk profiles, suggesting the need for an individualized approach when managing these conditions [8].

Genetic and molecular aspects

Genetic polymorphisms in single carbon metabolism genes (such as MTHFR C677T) can increase homocysteine and modulate the response to vitamin B12 supplementation [9].

Such preparations should be considered in patients with unexplained hyperhomocysteine or a strong family history of early vascular disease. These polymorphisms may explain the variation in who benefits most from B12 interventions.

Methods of giving supplements and practical effects

- Methods of administration: oral, intramuscular, and sublingual, and there are new delivery systems based on nanocarriers. Oral supplements are effective for most people, but intravenous administration is used for malabsorption.
- Doses: vary depending on the severity of the deficiency and the cause. Maintenance doses vary between nutritional deficiencies and absorption deficiencies.
- Safety: Vitamin B12 supplements are generally safe; excess is excreted by the kidneys. In rare cases, levels that are too high may serve as a negative diagnostic sign in hospitalized patients without being related to nutritional supplements [11].

Vitamin B12 supplements can be obtained through oral, intramuscular, or advanced delivery systems (nanotransporters). While oral supplements are sufficient for most patients, those with malabsorption syndromes or certain gastrointestinal disorders benefit from injectable administration. New methods for improving pharmacokinetics are under investigation but require further investigation [11].

Vitamin B12 in groups with chronic kidney disease (CKD) and high-risk cardiovascular disease

Patients with chronic kidney disease or end-stage renal disease usually have high homocysteine and a high prevalence of vitamin B12 deficiency. Vitamin B12 supplementation (particularly with concurrent folic acid) may reduce homocysteine and improve vascular outcomes in advanced chronic kidney disease; However, the reduction of clinical events is still under investigation, and optimal dosage/delivery (oral versus injection) is debated [10].

Limitations and controversy in clinical practice

- Not all studies show a reduction in cardiovascular events with homocysteine-lowering treatments, raising questions about causality versus association [4] ،[3].
- Benefits may be limited to those with documented deficiencies, but dietary supplements in patients who are not vitamin B12 deficient are unlikely to result in additional vascular benefits.
- Gender, age, genetics, comorbidities, drug interactions, and underlying nutritional status all influence B12 levels and clinical effects [8].

Although observational evidence links vitamin B12 status to cardiovascular disease risk, interventional studies provide mixed results regarding the effectiveness of supplementation in reducing clinical events. These discrepancies can be explained by patient choice (such as underlying deficiency condition), duration of intervention, or complex interaction between genetic and environmental factors [12]. However, it is clear that some subpopulations with severe deficiency or metabolic disorders benefit from targeted nutritional correction [7].

Clinical guidelines and recommendations

Although vitamin B12 status is an important indicator of cardiovascular and neurocognitive health, routine screening at the population level is not universally recognized. Clinical guidelines indicate regular monitoring in high-risk groups: the elderly, people with diabetes taking metformin, those with malabsorption or a history of bariatric or gastrointestinal surgery [6] ،[12]. Targeted supplements may improve metabolic indicators and reduce the risk of relapse in cases of secondary prevention.

Integrative and future considerations

- Personalized medicine: Genetic screening, sex-specific recommendations, and combination with other micronutrient assessments may enhance cardiovascular prevention and management strategies.
- Epigenetic impacts: More research is needed to clarify how vitamin B12 modulates gene expression related to atherosclerosis and metabolic syndrome [4].
- Advanced delivery systems: Nanotechnology and innovative oral preparations may enhance the effectiveness of nutritional supplements, especially in populations with absorption challenges [13]

Because deficiency is widespread, routine evaluation of vitamin B12 should be considered for cardiovascular patients, especially those with diabetes, elderly individuals, and those with renal impairment or receiving long-term treatment with metformin [13] .[14] .Treatment of confirmed deficiency may improve metabolic parameters, reduce the frequency of thrombotic events in selected patients, and support overall vascular health.

II. Recommendations

- **Screening Protocols**: Routine evaluation of vitamin B12 status should be implemented for cardiovascular patients, with particular emphasis on high-risk groups including diabetic patients on metformin, elderly individuals, and those with renal impairment or malabsorption syndromes.
- **Supplementation Strategies:** Oral supplementation proves effective for most patients; however, intramuscular administration is indicated for malabsorption syndromes. Dosage should be tailored based on deficiency severity and underlying etiology.
- **Monitoring Parameters**: Clinicians should monitor serum B12 levels, homocysteine concentrations, and lipid profiles, particularly in patients receiving long-term metformin therapy.

III. Conclusion

Vitamin B12 is integral to cardiovascular health by modulating homocysteine metabolism, lipid profiles, and possibly reducing cardiac metabolic risk. Its deficiency is common in at-risk populations and may exacerbate the development of cardiovascular diseases and their complications. Structured screening and targeted nutritional supplements, adapted to individual risk factors, promise improved outcomes in cardiovascular patients.

References

[1]. Mohan And Et Al, "Homocysteine, Vitamin B12 And Folate Level: Possible Risk Factors In The Progression Of Chronic Heart And Kidney Disorders," Current Cardiology Reviews, 2023.

[2]. Aleksandra And K. Zygmunt, "Hyperhomocysteinemia In Patients With Cardiovascular Disease," Index Copernicus International , 2014.

[3]. Y. Miao And Et Al, "The Effect Of B-Vitamins On The Prevention And Treatment Of Cardiovascular Diseases: A Systematic Review And Meta-Analysis," Nutrition Reviews , Pp. 1386-1401, 2023.

[4]. Kibirige And R. Mwebaze, "Vitamin B12 Deficiency Among Patients With Diabetes Mellitus: Is Routine Screening And Supplementation Justified?," Journal Of Diabetes & Metabolic Disorders, 2013.

[5]. L. Sarmiento-Rubiano And Et Al, "Relationship Between Vitamin B12 Levels And Insulin Resistance In Postmenopausal Women From Colombia Caribbean," Medicina (Ribeirao Preto), 2023.

A. Adaikalakoteswari And Et Al, "Vitamin B12 Deficiency Is Associated With Adverse Lipid Profile In Europeans And Indians With Type 2 Diabetes," Cardiovascular Diabetology, 2014.

[6]. J. Levy And Et Al, "Cardiovascular Manifestations Of Intermediate And Major Hyperhomocysteinemia Due To Vitamin B12 And Folate Deficiency And/Or Inherited Disorders Of One-Carbon Metabolism: A 3.5-Year Retrospective Cross-Sectional Study Of Consecutive Patients," American Journal Of Clinical Nutrition, Pp. 1157-1167, 2021.

[7]. M. Amini And Et Al, "Vitamin B12 Supplementation In End Stage Renal Diseases: A Systematic Review," Medical Journal Of The Islamic Republic Of Iran, Vol. 167, 2015.

[8]. B. Joseph And Et Al, "Low Vitamin B12 And Lipid Metabolism: Evidence From Pre-Clinical And Clinical Studies," Nutrients, 2020.

[9]. J. Wrblewska And Et Al, "Sex Differences In Vitamin Metabolism And Their Role In Oxidative Stress Regulation And Cardiometabolic Health," Nutrients, Vol. 16, P. 2697, 1 Aug 2025.

[10]. O. A. Abdelwahab And Et Al, "Efficacy Of Different Routes Of Vitamin B12 Supplementation For The Treatment Of Patients With Vitamin B12 Deficiency: A Systematic Review And Network Meta-Analysis," Irish Journal Of Medical Science, P. 1621–1639, 2024.

[11]. Zhang And Et Al, "Association Between B Vitamins Supplementation And Risk Of Cardiovascular Outcomes: A Cumulative Meta-Analysis Of Randomized Controlled Trials," Plos One, Vol. 9, P. 107060, 2014.

[12]. M. Hao And Et Al, "Nanoencapsulation Of Nutraceuticals: Enhancing Stability And Bioavailability In Functional Foods," Frontiers In Nutrition, P. 1746176, 2026.

[13]. Kibirige And R. Mwebaze, "Vitamin B12 Deficiency Among Patients With Diabetes Mellitus: Is Routine Screening And Supplementation Justified?," Journal Of Diabetes & Metabolic Disorders, Vol. 1, 2013.