

## What about B12 hypervitaminemia?

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Vitamin B12 is an essential nutrient involved in one-carbon metabolism and cell division. Daily intake of 2-5 µg, together with efficient absorption, transportation, and transformation, are needed to maintain health. In clinical practice, measurement of total plasma Cbl is requested widely for the biochemical assessment of Cbl deficiency. In clinical practice, the frequent occurrence of vitamin B12 deficiency, particularly in elderly patients, justifies systematic dosage of vitamin B12. High serum cobalamin level, which appears to be even more common than vitamin B12 deficiency, is therefore often only discovered fortuitously. *And what about hypervitaminemia B12?*

High serum levels of vitamin B12 or cobalamin, also called B12 hypervitaminemia, is a biological abnormality, yet one that is significantly underestimated. To date, no consensus on the management of this anomaly exists. According to the literature, high levels of vitamin B12 is associated or linked with a range of conditions, the majority of which are serious, with a systematic inquiry being decisive for prognosis following the discovery of high serum cobalamin levels. These conditions include solid neoplasia (whether metastatic or otherwise) and, either acute or chronic, malignant haematological disorders. Other causes include: mainly liver disorders and monoclonal gammopathy of undetermined significant and also renal failure; more rarely, excess vitamin B12 intake, inflammatory and auto-immune diseases, and transient haematological abnormalities (secondary neutrophilia or eosinophilia). Paradoxically, functional deficits including cobalamin deficiency are often associated with B12 hypervitaminemia. In our experience, using the chi-square or Fisher tests and the Student test, the factors with a significant link to hypervitaminemia B12 in univariate analysis were acute renal failure ( $p=0.0002$ ), liver diseases ( $p<0.0001$ ), and solid neoplasia ( $p=0.0030$ ). Using binary logistic regression for multivariate analysis, variables independently related to hypervitaminemia B12 were acute renal failure (odds ratio (OR)=6.3; 95% CI, 2.7-8.1;  $p<0.0001$ ), liver diseases (OR=5.4; 95% CI, 3.1-6.9;  $p<0.0001$ ), hematological disorders (OR=5.7;  $p=0.0017$ ), and age  $\geq 75$  years (OR=3.7; 95% CI, 1.9-4.8;  $p=0.0416$ ). Moreover, there is an apparent correlation between

rates of hypervitaminemia B12 and the number of etiologies identified.

In case of neoplasia, the major cancers that were implicated with B12 hypervitaminemia were hepatocellular carcinoma and secondary hepatic tumors, breast cancer, colon cancer, stomach cancer, and pancreatic tumors. The link between B12 hypervitaminemia and solid neoplasia was demonstrated by Carmel et al., in 1975 and 1977, when they studied vitamin B12 levels and vitamin B12 transporters in a population of 139 oncology patients. A high serum level of cobalamin has also been described as a potential marker for tumors with a poor prognosis. It has been suggested that vitamin B12 levels should be included in the decision-making process for oncological treatment and management, particularly for severely affected patients or for those who present with chronic conditions. Geissbühler et al., have attributed prognostic value to vitamin B12 in relation to tumor-based diseases. Accordingly, the BCI index (the product of B12  $\times$  CRP) represents a powerful predictor of mortality in relation to cancers in the palliative stages. Multiple studies confirm the significant link between B12 hypervitaminemia and liver disease. The pathophysiologic mechanism is an excess cobalamin release by the liver and the hepatic synthesis decrease of Transcobalamin II, which is essential for tissue fixation of B12 vitamin. High serum level of cobalamin has been confirmed as a compelling biological indicator for myeloproliferative disorders such as chronic myeloid leukemia, primitive polyglobulism, essential thrombocythemia and other myelofibrosis. Elevated plasma Cobalamin levels have also been associated with several nonmalignant diseases, including liver diseases, alcoholism, and renal, autoimmune, and infectious diseases.

The vitamin B12 level can be an early marker in diagnosing these conditions. Its use as a potential predictor of mortality in geriatric medicine requires further study. The coexistence of multiple possible etiologies that may explain hypervitaminemia means that a standardized assessment is indispensable in order to ensure that no condition is overlooked and to enable the formulation of a treatment program adapted to the individual patient.

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