Nutrition Reviews

Special Article

How prevalent is vitamin B_{12} deficiency among vegetarians?

Roman Pawlak, Scott James Parrott, Sudha Raj, Diana Cullum-Dugan, and Debbie Lucus

Vegetarians are at risk for vitamin B_{12} (B12) deficiency due to suboptimal intake. The goal of the present literature review was to assess the rate of B12 depletion and deficiency among vegetarians and vegans. Using a PubMed search to identify relevant publications, 18 articles were found that reported B12 deficiency rates from studies that identified deficiency by measuring methylmalonic acid, holo-transcobalamin II, or both. The deficiency rates reported for specific populations were as follows: 62% among pregnant women, between 25% and almost 86% among children, 21–41% among adolescents, and 11–90% among the elderly. Higher rates of deficiency were reported among vegans compared with vegetarians and among individuals who had adhered to a vegetarian diet since birth compared with those who had adopted such a diet later in life. The main finding of this review is that vegetarians develop B12 depletion or deficiency regardless of demographic characteristics, place of residency, age, or type of vegetarian diet. Vegetarians should thus take preventive measures to ensure adequate intake of this vitamin, including regular consumption of supplements containing B12.

INTRODUCTION

Vitamin B_{12} (B12) has the largest and most complex chemical structure of all vitamins.[1] It is named cobalamin because cobalt is a part of its chemical structure. Cobalamin belongs to a group of cobalt-containing compounds known as corrinoids.[2,3] Some of these compounds are biologically inactive in humans, while methylcobalamin and adenosylcobalamin are biologically active. Hydroxycobalamin and cyanocobalamin constitute two additional forms that may be metabolized into either methylcobalamin or adenosylcobalamin and can thus play functional roles in human cells.

B12 is an essential nutrient important in transferring the methyl group in a methionine synthase-requiring reaction, which converts homocysteine to methionine. This reaction activates folate, which can be utilized in DNA synthesis. B12 is also needed in the synthesis of myelin and thus the maintenance and repair of neural axons. In addition, B12 is essential for the synthesis of energy in mitochondria and for erythropoiesis in bone marrow.[4,5]

B12 is only synthesized by microorganisms and is, thus, not found in foods of plant origin, except through contamination with soil or by exposure to foods containing B12, such as milk solids during processing or in foods fortified with this vitamin.[3,6] Since vegetarians have limited natural sources of B12 (milk, dairy, and eggs), the presence of B12 in plant-based diets depends on the inclusion/exclusion of foods of animal origin, consumption of foods fortified with B12, or the use of B12 supplements. Although B12 deficiency was once thought to be extremely rare except among strict vegetarians, it is now known that B12 deficiency is relatively common among

Affiliations: *R Pawlak* is with the Department of Nutrition Science, East Carolina University, North Carolina, USA. *SJ Parrott* is with the Department of Nutritional Sciences, School of Health Related Professions, University of Medicine and Dentistry of New Jersey, Newark, New Jersey, USA. *S Raj* is with the Department of Public Health, Food Studies and Nutrition, Syracuse University, Syracuse, New York, USA. *D Cullum-Dugan* is with Namaste Nutrition, Watertown, Massachusetts, USA. *D Lucus* is with the Sutter Medical Foundation, Roseville, California, USA.

Correspondence: *R Pawlak*, Department of Nutrition Science, East Carolina University, Rivers West 337, Greenville, NC 27858, USA. E-mail: pawlakr@ecu.edu. Phone: +1-252-328-2350.

Key words: cobalamin, deficiency, vegetarians, vegans, vitamin B_{12}

doi:10.1111/nure.12001

people adhering to all types of vegetarian diets, including lacto-ovo-vegetarian, and other population subgroups, such as the elderly.[7,8]

Although a variety of assessment techniques have been used to assess B12 status, e.g., serum or plasma B12, mean corpuscular volume (MCV), homocysteine (tHcy), holo-transcobalamin II (holo-TCII), and serum or urinary methylmalonic acid (MMA), the newest research findings indicate that MMA and holo-TCII are the most accurate, while serum or plasma B12 and MCV are unreliable.[3,5,9] Herbert[9] suggested that holo-TCII shows a degree of B12 depletion while MMA indicates the extent of deficiency. He further indicated that the progression from normal B12 status to deficiency passes through a stage called depletion and that holo-TCII is the best marker of this stage, while MMA is the best marker of B12 status when stores are exhausted and deficiency has been reached.[9] Herbert (as well as others) also suggested that more than one assessment technique should be used to determine B12 status. As reported by Antony,[10] researchers who reported B12 status among vegetarians based on the use of serum B12 level as a marker of B12 status likely underestimated the rate of deficiency due to the inherent inaccuracy of this assessment method. The goal of the present review was to assess B12 depletion and deficiency among people adhering to different types of vegetarian diets based on studies that reported B12 status from measurements of serum holo-TCII and/or serum or urinary MMA.

To achieve this goal, a PubMed search was performed using the following key words: B12, cobalamin, vegetarians, vegans, and deficiency. The titles and abstracts of the resulting publications were then screened to identify manuscripts in which reports of B12 status among vegetarians were based on the use of holo-TCII, MMA, or both. The reference lists of manuscripts selected initially were then checked to search for additional manuscripts that may not have been identified in the initial PubMed search. Research manuscripts that reported the use of either of the two assessment techniques, but reported only means or medians without percentages of the sample with abnormal values, were excluded.

RESULTS

A total of 18 manuscripts meeting the inclusion criteria were identified.[11–28] The studies included very heterogeneous samples that incorporated pregnant women,[14] infants,[27] children,[24,26] adolescents,[11,23,28] adults, and the elderly.[12,13,15–26] They included male and female participants who adhered to different types of vegetarian diets: semi-vegetarian, macrobiotic, lacto-vegetarian (LV) or lacto-ovo-vegetarian (LOV), vegan, and vegan raw food. Two of the reviewed manuscripts utilized urinary MMA, eight used serum MMA, one used both urinary and serum MMA, while seven reported the use of both MMA and holo-TCII (four of these studies reported separate rates for depletion and deficiency, while three described a rate for participants who had both low holo-TCII and elevated MMA). Assessment of what constituted deficiency was the same across studies for holo-TCII (<35 pmol/L) and urinary MMA (>4.0 μg/mg creatinine), while the serum MMA cutoff value varied widely, from >260 μmol/L to >0.75 μmol/L. Assessment subjects included individuals of various ethnic backgrounds and living in a variety of countries, such as China (including Hong Kong),[21,22] Germany,[13,16–20,24] Ethiopia,[14] India,[25] New Zealand,[26] the Netherlands,[11,16,19,24,28] Norway,[27] Oman,[17] and the United States.[23]

Pregnant women

Only one of the studies included pregnant women.[14] This study was conducted in Ethiopia and included participants whose diet was based on either maize or enset. The reported prevalence of B12 deficiency, defined as MMA >271 nmol/L, was 62%.

Infants and children

One study reported the prevalence of B12 deficiency among 41 Norwegian infants.[27] Deficiency (MMA >0.43 μmol/L) was detected among 85.4% of the sample. Two studies, one from the United States[23] and the other from New Zealand (evaluating Asian Indian migrants),[26] examined the prevalence of B12 deficiency among children. The American children followed a macrobiotic diet, while the Asian Indians in New Zealand were LOVs. The prevalence of B12 deficiency was estimated to be 55% among US children (67% among children who followed a vegetarian diet all their life versus 25% among other vegetarian children) and 50% among children of Asian Indian origin. B12 deficiency was defined as urinary MMA >4.0 mmol/mol creatinine in the US study and serum MMA >430 nmol/L in the New Zealand study.

Adolescents

Two of the reviewed studies assessed B12 deficiency among children and adolescents (ages 9–15 years).[11,28] In both cases, participants adhered to a macrobiotic diet in the first 6 years of their lives and subsequently switched to an LV, LOV, or omnivorous diet. Prevalence of deficiency was 41% in one of the two studies, with deficiency defined as MMA >290 nmol/L; in the other study, deficiency prevalence was 21% with deficiency defined as MMA >410 nmol/L.

Adults and the elderly

Twelve studies assessed B12 deficiency in non-pregnant adults, including young adults and the elderly.[12,13,15–25] The prevalence of depletion or deficiency was reported as follows: 32% and 43% among young adult LVs or LOVs and vegans, respectively, with deficiency defined as MMA >271 nmol/L; 47% among raw food vegans, with deficiency defined as MMA >4.0 μg/mg creatinine; from 30% through 76% of adults depending on the definition of deficiency (MMA >4.0 μg/mg creatinine versus MMA >0.260 μmol/L); and 90% among vegans (depletion defined as holo-TCII <35 pmol/L). Prevalence among vegans in the United Kingdom was 11%. However, the criterion for deficiency used in this study was two to three times higher than in most other studies.

Detailed features of the studies, including rates of depletion and deficiencies, are listed in Table 1.

DISCUSSION

In this review, the rates of B12 depletion and deficiency were assessed through an evaluation of published studies that included participants adhering to different types of vegetarian diets. One of the main findings is that vegetarians develop B12 deficiency (assessed with holo-TCII, MMA, or both) regardless of demographic characteristics, place of residency, age, or the type of vegetarian diet consumed. In the past, it was assumed that only strict vegetarians (vegans) were at risk for B12 deficiency, but for some time now, and as this review confirms, it has been known that not only vegans commonly develop B12 depletion or deficiency.[7,8,29] Depending on the criterion used, the prevalence of B12 depletion or deficiency among vegetarians ranged from about 11 to 90%. Lower rates were reported in studies that used less stringent deficiency criteria (e.g., MMA >0.75 μmol/L vs >0.271 μmol/L) and in studies in which participants met two different deficiency criteria (e.g., low holo-TCII and elevated MMA). In three of the four studies that reported rates of depletion (low holo-TCII) and deficiency (elevated MMA) separately, the rate was higher for holo-TCII than for MMA.

The deficiency rate among infants and children was at least equal to that of adults and the elderly. Higher rates were reported among children who followed a vegetarian lifestyle from birth, compared to those who adopted it later in life.[17,23] This finding is likely due to low maternal B12 stores that resulted in low stored B12 in offspring during infancy and childhood.

Two of the reviewed studies reported B12 deficiency separately among LVs or LOVs and vegans.[18,19] Herrmann et al. 2001[18] found that 32% of the LOVs and LVs were B12 deficient, while the rate was 43% among vegans. Herrmann et al. 2003[19] additionally found that 31% of the LOVs and LVs who took B12-containing supplements were deficient, compared to 68% of LOVs and LVs who did not take such supplements. Surprisingly, the rate of deficiency was higher among vegans who used B12-containing supplements (88%) than among those who did not use them (83%). On the other hand, in a study by Gilsing et al.,[15] the prevalence of B12 deficiency was the lowest (11%) among vegans, 19% of whom used B12 supplements.[15] However, Gilsing et al.,[15] used the least stringent criteria of B12 deficiency (MMA >0.75 μmol/L versus 271 nmol/L in several other studies). The fact that even supplement users were diagnosed with deficiency may be due to two factors: 1) using them less frequently than needed and 2) using supplements with a lower dose than needed to maintain adequate B12 status. While supplements have been shown to be effective in correcting B12 deficiency,[10,12,30,31] according to one study, the dose of B12 in a supplement should be about 100 times higher than the RDA.[3] Also, in cases of deficiency, a dose that is at least 200 times higher than the RDA may need to be ingested to achieve the most desirable results.[32]

Although B12 deficiency is associated with a host of adverse symptoms, Herrmann et al.,[17] indicated that none of the vegetarians included in their study had clinical symptoms despite the fact that about two-thirds of the sample had B12 depletion or deficiency, as indicated by both low holo-TCII and elevated MMA. According to the stages of B12 deficiency developed by Herbert,[9] although this is not always the case, clinical manifestations of B12 deficiency (stage IV) develop after biochemical deficiency is present (stage III). In addition, Herbert suggested that low holo-TCII is an indication of B12 depletion and elevated MMA indicates a deficiency.[9] Thus, symptoms of deficiency, at least the severe symptoms, may not be seen with low values of holo-TCII or even in higher-than-normal values of MMA. However, one has to be careful with concluding that biochemical indicators of B12 deficiency in vegetarians are not associated with any adverse symptoms. Deficiency symptoms of this vitamin may be mild to severe. Mild symptoms, such as lethargy or forgetfulness may not even be detected or may be associated with other issues, such as aging or tiredness due to other reasons. One should also keep in mind that even some hematological symptoms, such as elevated mean corpuscular volume of erythrocytes, may not be shown in biochemical assessments. This is because such symptoms may be masked by either iron deficiency or high intake of folate. Vegetarians are more likely to have both. In addition, Herbert suggested that while it may take a relatively long time for B12 stores to be depleted, once depleted, symptoms of deficiency, of which some are irreversible, may occur rapidly.[9] Furthermore, Herrmann and Geisel[33] suggested that the function of B12-dependent enzymes,

Table 1 **Summary of studies evaluating vitamin B_{12} status of vegetarians.**

Reference	Country	Participants	Diet duration	Assessment criteria used	Rate of deficiency
Dhonukshe-Rutten et al. (2005)[11]	Netherlands	*N* = 73 formerly macrobiotic adolescents who switched mostly to vegetarian diet at mean age of 6.2 y Age range: 9–15 y	From birth until mean age of 6.2 y macrobiotic diet; thereafter, LV, LOV, or omnivorous diet	Serum MMA: >0.29 µmol/L	41%
Donaldson (2000)[12]	USA	*N* = 49 raw food vegans (17 men and 32 women) Mean age (SD): 55 y (9)	23–49 months	Urinary MMA: >4.0 µg/mg creatinine	47%
Geisel et al. (2005)[13]	Germany	*N* = 71 apparently healthy vegetarians; 48 LOVs(mean age: 53 y) and 23 vegans (mean age: 51 y)	Criteria for inclusion: >1 year on vegetarian diet	Holo-TCII: <35 pmol/L Serum MMA: >271 nmol/L	58% with deficiency defined as having met both holo-TCII and MMA criteria
Gibson et al. (2008)[14]	Ethiopia	*N* = 99 pregnant women, who consumed a maize- or an enset-based diet Mean age (SD): 27.8 y (4.6)	Not reported	Serum MMA: >271 nmol/L	62%
Gilsing et al. (2010)[15]	United Kingdom	*N* = 65 vegan men Mean age (SD): 42.8 y (13.1)	Median of 7 years	Holo-TCII: <35 pmol/L Serum MMA: >0.75 µmol/L	Holo-TCII: 40% Serum MMA: 11%
Herrmann et al. (2003)[16]	Germany and the Netherlands	*N* = 111 (56 female and 55 males) Mean age: 46 y		Holo-TCII: <35 pmol/L MMA: >271 nmol/L	Holo-TCII: 72% MMA: 60%; 55% had combined low levels of holo-TCII and elevated MMA
Herrmann et al. (2009)[17]	Oman (German and Asian-Indian immigrants)	*N* = 96 vegetarian males (23 German vegans, 54 German and 19 Asian Indian LOs or LOVs) Mean age (range): 50 y (36–70 y)	At least 2 years for Germans and from birth for Asian Indians	Holo-TCII: <35 pmol/L MMA: >271 nmol/L	66% of Germans and 69% of Asian Indians according to MMA and holo-TCII
Herrmann et al. (2001)[18]	Germany	*N* = 34 LVs or LOVs and N = 7 vegans Median age (range): 22 y (19–56 y)	Inclusion criteria: following the dietary pattern for ≥ 1 year	MMA: >271 nmol/L	32% of LVs or LOVs 43% of vegans
Herrmann et al. (2003)[19]	Germany and the Netherlands	*N* = 66 LVs or LOVs (53 of whom were B12 supplements users) Mean age (range): 48 y (24–75 y) *N* = 29 vegans (17 of whom were B12 supplements users) Mean age (range): 37 y (15- 64 y)	Inclusion criteria: following the dietary pattern for ≥ 1 year	Holo-TCII: <35 pmol/L MMA: >271 nmol/L	Holo-TCII: 73% of LVs or LOVs and 90% of vegans MMA: 61% of LVs or LOVs and 86% of vegans

Table 1 **Continued**

Reference	Country	Participants	Diet duration	Assessment criteria used	Rate of deficiency
Herrmann et al. (2005)[20]	Germany	$N = 50$ vegans Median age (range): 44 y (20–66 y) $N = 114$ LVs or LOVs Median age (range): 50 y (35–71 y)	Not reported	Holo-TCII: <35 pmol/L MMA: >271 nmol/L	Holo-TCII: 61% of LVs or LOVs and 76% of vegans MMA: 57% of LVs or LOVs and 74% of vegans
Kwok et al. (2002)[21]	China	$N = 119$ Chinese women Age: >55 years	>3 years	MMA: ≥ 0.4 μmol/L Serum B12: <150 pmol/L	Definite deficiency: 42% (vitamin B12 level <150 pmol/L and MMA 0.4 μmol/L) Possible deficiency: 32.8% (either criterion)
Kwok et al. (2004)[22]	Hong Kong	$N = 113$ female Chinese vegetarians Age: >55 years	Not reported	Serum MMA: >0.4 μmol/L Urinary MMA: μg/mg creatinine	Serum MMA: 32% Urinary MMA: 81%
Miller et al. (1991)[23]	United States (New England)	$N = 110$ adults Age range: 21–70 y $N = 42$ children Age range: 1.5–11.7 y All subjects followed a macrobiotic vegetarian diet	Adults: 1–379 months with a median of 41 months Children: 8–48 months, with a median of 27 months; 30 of 42 children adhered to the diet since weaning	4.0 mmol/mol creatinine	Adults: 30% Children: 55% (67% among children who followed a vegetarian diet all their life versus 25% among other vegetarian children)
Obeid et al. (2002)[24]	Germany and the Netherlands	$N = 111$ (29 vegans, 64 LVs or LOVs, and 20 semi-vegetarians defined as eating meat once weekly; 49 males and 64 females); Mean age (SD): 46 y (15)	Not reported	MMA: >271 nmol/L	Unclear. Figure shows 58% but text reports 85%
Refsum et al. (2001) [25]	India	$N = 78$, mostly LOVs Age range: 27–55 y	Most of their life	Holo-TCII: <35 pmol/L MMA: >0.260 μmol/L	Holo-TCII: 75% MMA: 76%
Rush et al. (2009)[26]	New Zealand	$N = 6$ pre-pubertal Indian girls who migrated to New Zealand Age range: 9–11 y	From birth	MMA: >0.26 μmol/L	50%
Schneede et al. (1994)[27]	Norway	$N = 41$ infants (22 boys and 19 girls) Mean age (range): 16.8 months (11.4–21.9 months)	From birth	MMA: >0.43 μmol/L	85.4%
van Dusseldorp et al. (1999)[28]	The Netherlands	$N = 73$ adolescents (36 boys and 37 girls) fed a macrobiotic vegan diet early in life, and currently LV Age range: 9–15 y	Macrobiotic diet from birth until mean age of 6.4 y and LV, LOV, or omnivorous diet since then	MMA: >0.41 mmol/L	21%

Abbreviations: LOV, lacto-ovo-vegetarian; LV, lacto-vegetarian.

methionine synthase and methylmalonyl-CoA mutase, are already impaired at stage III deficiency. This may lead to a variety of problems, including hyperchomocysteinemia, which is associated with many health problems.[2]

Food sources of B12

The Institute of Medicine's recommended dietary allowance (RDA) of B12 needed to meet an adult's requirement as 2.4 µg per day. B12 is synthesized only by microorganisms, and this is why natural food sources of B12 are limited to meats and foods of animal origin. Clams and beef liver are the highest sources of B12, containing about 84 and 71 µg of B12 in a 3 oz serving.[6] The amount of B12 found in a chicken varies from about 3.3 µg in the entire chicken liver to 0.03 µg in a chicken's neck.[6] Pork contains between 0.3 µg of B12 in each sausage patty to about 11.4 µg in pork liver.[6] The content of B12 in fish ranges from about 9 µg in one half of a fillet of sockeye salmon to about 0.5 µg in a 3 oz serving of yellowfin tuna.[6]

Vegetarian sources of B12 include milk, which contains between 0.3 and 0.4 µg/100 g of B12, with an absorption rate of about 65%. The B12 content of cheese or cottage cheese ranges from 20 to 60% that of milk. The amount of B12 in a whole egg is between 0.9 and 1.4 µg/100 g. B12 can be destroyed by heat and, thus, boiling milk can destroy 30–50% of B12, depending on the duration of cooking.[2,6,34]

In the United States, many commercial food products are fortified with B12, including a variety of breakfast cereals, soy milk, and certain soy meat analogs. These foods contain B12 in amounts ranging from less than the RDA to more than 200% of the RDA.

Supplements and fortified foods. In the United States and some other countries, pharmacies and health food stores alike offer B12-containing supplements, mostly as cyanocobalamin. Other forms of this vitamin, such as methylcobalamin and hydroxycobalamin, are also available. The doses of cyanocobalamin used in supplements include 100, 250, 500, 1,000, 3,000 and 5,000 µg. Nutritional yeast may also be fortified with B12, and approximately two tablespoons typically contains the amount equal to the US RDA. Results of a study conducted by Donaldson[12] showed, however, that supplements were more effective than nutritional yeast in correcting deficiency.

Prevention and treatment of deficiency

Vegetarians have very limited and vegans have no food sources that naturally contain B12.[2] Biochemical values of B12 deficiency among vegetarians correlate with B12 intake.[23,33] While it is theoretically possible to ingest an adequate amount of B12 from milk, dairy products, and eggs or from foods fortified with B12, not all vegetarians and few vegans consume the required amount of these products. Also, as indicated by this review, B12 deficiency is common among people adhering to all types of vegetarian diets, which could indicate that adequate intake might be much harder to achieve than it may seem or that other factors, in addition to relatively low intake, play a role in deficiency development. It should be emphasized that a study performed in the New England region of the United Stated found that deficiency among macrobiotic vegans reached 30% in adults and 55% in children.[23] This is important because many foods including cereal or soy products are fortified with B12 in this country. Thus, while B12 deficiency can theoretically be avoided by consuming milk, dairy, eggs, foods fortified with B12 and by using nutritional yeast, a prudent strategy to prevent B12 deficiency should include the use of B12 supplements. Supplements, when taken in an adequate dose, are very effective in both the prevention and treatment of B12 deficiency and are very cost effective.[12] However, many vegetarians, for different reasons, refuse to take B12 supplements.[29] This is largely due to various misconceptions, including the belief that it takes many years for B12 deficiency to develop.[7] This belief assumes that most people have adequate stores of B12[9]; however, this is very unlikely, especially in long-term vegetarians and vegans. Results of studies that included either Asian Indians or children consuming a macrobiotic diet, with both groups consuming a vegetarian diet from birth, showed they had higher rates of B12 deficiency than subjects who adhered to vegetarianism for a shorter time period.[17,25]

Studies do not support the position that it takes up to 20 or 30 years to develop a deficiency.[7] According to Donaldson,[12] 47% of the sample developed a deficiency, and most of these individuals had adhered to a raw vegan diet for between 23 and 49 months or about 2–4 years. In a study conducted by Herrmann et al.[17] 66% of German participants who had adhered to a vegetarian diet for at least 2 years were found to be B12 deficient.

A healthy enterohepatic circulation is needed for efficient B12 absorption.[9] B12 is secreted with bile and can be reabsorbed. As pointed out by Herbert,[9] the rate of reabsorption of B12 can reach up to 100%; however, B12 can only be reabsorbed in the presence of intrinsic factor. Vegetarians can be considered a group at high risk for atrophic gastritis, which affects intrinsic factor synthesis. This is, in part, due to the fact that vegetarians are at higher risk for iron deficiency. Iron deficiency can contribute to gastric mucosa damage, which leads to atrophic gastritis. Atrophic gastritis is associated with synthesis of weaker hydrochloric acid and an inability to synthesize intrinsic factor. Both conditions can lead to a reduced or absent ability to absorb B12.

Many people who adopt a vegetarian or vegan lifestyle do so for health reasons. Since B12 deficiency is associated with higher risk of some of the very health conditions vegetarians are trying to avoid (e.g., occlusive vascular disease, Alzheimer's disease/dementia, osteoporosis, etc.),[35,36] this knowledge might encourage vegetarians to take B12 supplements. Thus, public health campaigns targeting vegetarians should include messages conveying the risk of developing specific health conditions due to B12 deficiency.

Some scientists have proposed that flour be fortified with B12. Fortification of flour with folic acid contributed to increases in the folic acid content of red blood cells, decreases in total homocysteine, and consequent reductions in rates of neural tube defects.[37] It is reasonable to assume that a similar preventive measure with B12 would have the same effect in terms of reducing rates of B12 deficiency. B12 deficiency is associated with a variety of health issues, including low mineral density,[17] increased risk for heart disease,[35,36] and neural tube defects.[35,36] Thus, the fortification of flour with B12 could prove to be the most cost-effective solution in terms of prevention of these and other B12 deficiency-related symptoms and conditions.

CONCLUSION

The present review of the literature regarding B12 status among vegetarians shows that the rates of B12 depletion and deficiency are high. It is, therefore, recommended that health professionals alert vegetarians about the risk of developing subnormal B12 status. Vegetarians should also take preventive measures to ensure adequate intake of this vitamin, including the regular intake of B12 supplements to prevent deficiency. Considering the low absorption rate of B12 from supplements, a dose of at least 250 μg should be ingested for the best results.[3]

Acknowledgments

All authors met the authorship criteria specified in the guidelines for authors and no person was omitted from the list of authors.

Declaration of interest. The authors have no relevant interests to declare.

REFERENCES

1. Smith E. Purification of anti-pernicious anemia factors from liver. Nature. 1948;161:638–639.
2. Watanabe F. Vitamin B12 sources and bioavailability. Exp Biol Med. 2007;232:1266–1274.
3. Herbert V. Vitamin B-12: Plant sources, requirements, and assay. Am J Clin Nutr. 1988;48:852–858.
4. National Institutes of Health. *Genetics Home Reference: MUT*. 2012; Available at: http://ghr.nlm.nih.gov/gene/MUT. Accessed 30 November 2012.
5. Institute of Medicine of the National Academies. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline*. 2000; Available at: http://www.iom.edu/Reports/2000/Dietary-Reference-Intakes-for-Thiamin-Riboflavin-Niacin-Vitamin-B6-Folate-Vitamin-B12-Pantothenic-Acid-Biotin-and-Choline.aspx. Accessed 10 September 2010.
6. USDA National Nutrient Database for Standard Reference, Release 18. *Vitamin B12 (μg) Content of Selected Foods Per Common Vitamin B-12 Measure, Sorted by Nutrient Content*. 2005; Available at: http://www.nal.usda.gov/fnic/foodcomp/Data/SR18/nutrlist/sr18w418.pdf. Accessed 27 November 2011.
7. Allen LH. How common is vitamin B12 deficiency? Am J Clin Nutr. 2009;89(Suppl):S693–S696.
8. Stabler SP, Allen RH. Vitamin B12 deficiency as a world-wide problem. Annu Rev Nutr. 2004;24:299–326.
9. Herbert V. Staging vitamin B-12 (cobalamin) status in vegetarians. Am J Clin Nutr. 1994;59(Suppl):S1213–S1222.
10. Antony AC. Vegetarianism and vitamin B-12 (cobalamin) deficiency. Am J Clin Nutr. 2003;78:3–6.
11. Dhonukshe-Rutten RA, van Dusseldorp M, Schneede J, et al. Low bone mineral density and bone mineral content are associated with low cobalamin status in adolescents. Eur J Nutr. 2005;44:341–347.
12. Donaldson MS. Metabolic vitamin B12 status on a mostly raw vegan diet with follow-up using tablets, nutritional yeast, or probiotic supplements. Ann Nutr Metab. 2000;44:229–234.
13. Geisel J, Schorr H, Bodis M, et al. The vegetarian lifestyle and DNA methylation. Clin Chem Lab Med. 2005;43:1164–1169.
14. Gibson RS, Abebe Y, Stabler S, et al. Zinc, gravida, infection, and iron, but not vitamin B-12 or folate status, predict hemoglobin during pregnancy in Southern Ethiopia. J Nutr. 2008;138:581–586.
15. Gilsing AM, Crowe FL, Lloyd-Wright Z, et al. Serum concentrations of vitamin B12 and folate in British male omnivores, vegetarians and vegans: Results from a cross-sectional analysis of the EPIC-Oxford cohort study. Eur J Clin Nutr. 2010;64:933–939.
16. Herrmann W, Obeid R, Schorr H, et al. Functional vitamin B12 deficiency and determination of holotranscobalamin in populations at risk. Clin Chem Lab Med. 2003;41:1478–1488.
17. Herrmann W, Obeid R, Schorr H, et al. Enhanced bone metabolism in vegetarians – the role of vitamin B12 deficiency. Clin Chem Lab Med. 2009;47:1381–1387.
18. Herrmann W, Schorr H, Purschwitz K, et al. Total homocysteine, vitamin B12, and total antioxidant status in vegetarians. Clin Chem. 2001;47:1094–1101.
19. Herrmann W, Schorr H, Obeid R, et al. Vitamin B-12 status, particularly holotranscobalamin II and methylmalonic acid concentrations, and hyperhomocysteinemia in vegetarians. Am J Clin Nutr. 2003;78:131–136.
20. Herrmann W, Obeid R, Schorr H, et al. The usefulness of holotranscobalamin in predicting vitamin B12 status in different clinical settings. Current Drug Metabolism. 2005;6:47–53.
21. Kwok T, Cheng G, Woo J, et al. Independent effect of vitamin B12 deficiency on hematological status in older Chinese vegetarian women. Am J Hematol. 2002;70:186–190.
22. Kwok T, Cheng G, Lai WK, et al. Use of fasting urinary methylmalonic acid to screen for metabolic vitamin B12 deficiency in older persons. Nutrition. 2004;20:764–768.
23. Miller DR, Specker BL, Ho ML, et al. Vitamin B-12 status in a macrobiotic community. Am J Clin Nutr. 1991;53:524–529.
24. Obeid R, Geisel J, Schorr H, et al. The impact of vegetarianism on some haematological parameters. Eur J Haematol. 2002;69:275–279.
25. Refsum H, Yajnik CS, Gadkari M, et al. Hyperhomocysteinemia and elevated methylmalonic acid indicate a high prevalence of cobalamin deficiency in Asian Indians. Am J Clin Nutr. 2001;74:233–241.
26. Rush EC, Chhichhia P, Hinckson E, et al. Dietary patterns and vitamin B12 status of migrant Indian preadolescent girls. Eur J Clin Nutr. 2009;63:585–587.
27. Schneede J, Dagnelie PC, van Staveren WA, et al. Methylmalonic acid and homocysteine in plasma as indicators of functional cobalamin deficiency in infants on macrobiotic diets. Pediatr Res. 1994;36:194–201.
28. Van Dusseldorp M, Schneede J, Refsum H, et al. Risk of persistent cobalamin deficiency in adolescents fed a macrobiotic diet in early life. Am J Clin Nutr. 1999;69:664–671.
29. Anthony A. Vegetarianism and vitamin B-12 (cobalamin) deficiency. Am J Clin Nutr. 2003;78:3–6.
30. Evatt ML, Terry PD, Zoegler TR, et al. Association between vitamin B12-containing supplement consumption and prevalence of biochemically defined B12 deficiency in adults in NHANES III (Third National Health and Nutrition Examination Survey). Public Health Nutr. 2010;13:25–31.
31. Aroni K, Anagnostopoulou K, Tsagroni E, et al. Skin hyperpigmentation and increased angiogenesis secondary to vitamin BI2 deficiency in a young vegetarian woman. Acta Derm Venereol. 2008;88:191–192.

32. Eussen SJ, de Groot LC, Clarke R, et al. Oral cyanocobalamin supplementation in older people with vitamin B12 deficiency. Arch Intern Med. 2005;165:1167–1172.
33. Herrmann W, Geisel J. Vegetarian lifestyle and monitoring of vitamin B-12 status. Clin Chim Acta. 2002;326:47–59.
34. Squires MW, Naber EC. Vitamin profiles of eggs as indicators of nutritional status in the laying hen: Vitamin B12 study. Poult Sci. 1992;71:275–282.
35. Malizia RW, Baumann BM, Chansky ME, et al. Ambulatory dysfunction due to pernicious anemia. J Emerg Med. 2010;38:302–307.
36. Stabler SP, Allen RH, Savage DG, et al. Clinical spectrum and diagnosis of cobalamin deficiency. Blood. 1990;76:871–881.
37. Pfeiffer CM, Caudill SP, Gunter EW, et al. Biochemical indicators of B vitamin status in the US population after folic acid fortification: Results from the National Health and Nutrition Examination Survey 1999–2000. Am J Clin Nutr. 2005;82:442–450.