The prevalence of cobalamin deficiency among vegetarians assessed by serum vitamin B12: a review of literature

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INTRODUCTION

Vitamin B12 is a water-soluble vitamin that is found naturally in meat and animal products. It contains a corrin ring with mineral cobalt. Physiologic functions of vitamin B12 include erythropoiesis, the synthesis and maintenance of myelin sheath and the synthesis of nucleic acid (DNA).1,2 The current Recommended Dietary Allowance for vitamin B12 has been set by the Institute of Medicine at 2.4 μg per day for male and female subjects, aged 14 years and older.2 Recommended intake amounts depend on age and physiological development and range from 0.4 μg in infants 6.6 to 2.8 μg per day in pregnant and lactating women, respectively.1

According to data from 1999 to 2000 National Health and Nutrition Examination Survey, the median daily intake of vitamin B12 in the United States is 3.4 μg.1 Although this amount is higher than the recommended intake, deficiency of vitamin B12 can be seen in high-risk individuals.1,6 These individuals include older adults and the elderly, individuals with gastrointestinal disorders or those who have undergone gastrointestinal surgery and individuals following a vegetarian or vegan diet.1,2,5,6 Clinical symptoms of deficiency include fatigue, weakness, constipation, loss of appetite, weight loss, numbness and tingling in hands and feet, difficulty maintaining balance, depression, confusion, dementia, poor memory and soreness of the mouth or tongue.1,2,6

Many individuals who adhere to vegetarian diets and do not use vitamin B12 supplements can develop vitamin B12 deficiency, regardless of the type of vegetarian diet they consume.7 This is in part due to the fact that plant products do not naturally contain vitamin B12.1,5,6 Vegans, who do not ingest any foods of animal origin, are at the highest risk of developing a deficiency. Vegetarians, other than vegans, consume some foods that are a natural source of vitamin B12 (e.g. milk, yoghurt, cheese, eggs). Still, even they have limited natural sources of this vitamin.2 Even though some foods such as cereal or soy products are fortified with vitamin B12, studies have shown that vegetarians often have suboptimal vitamin B12 intake.2,7

The aim of this review was to assess the prevalence of vitamin B12 deficiency among individuals adhering to vegetarian diets. The review is based on studies that reported percentage of vitamin B12 deficiency assessed by serum vitamin B12.

MATERIALS AND METHODS

A systematic literature search was carried out using multiple internet-based search engines including PubMed, Medline, CINAHL plus, ERIC, Nursing and Allied Health Collection and Nursing/Academic Edition. To identify relevant literature, a title search was used.2,7 Using combinations of the following key words was used, ‘B12’, ‘cobalamin’, ‘vegetarian’, ‘vegan’ and ‘deficiency’. Following the literature search, the titles and abstracts of the manuscripts were screened to assess the eligibility of identified manuscripts. Inclusion criteria consisted of original studies that assessed serum vitamin B12 concentration, were written in English, were non-case studies and studies that reported actual percentages of vitamin B12 deficiency. Studies that reported serum vitamin B12 values such as means or medians but did not report the prevalence of deficiency in their samples were excluded.
RESULTS

The literature search yielded a total of 1097 manuscripts. One thousand and fifty-seven studies were excluded because they did not meet the inclusion criteria. Thus, 40 studies remained and were included in the review.8–47 The samples included in these studies consisted of a wide range of individuals at different life stages, including infants,47 children and adolescents,12,14,22,25,31 pregnant women,18 adults,10,12,13,15,24,26,28,30–32,39–41 and the elderly.11,12,40

Most studies included both sexes, but 10 studies assessed vitamin B12 status in female subjects only,8,17,21,24,25,33,40,41,45 and three included male subjects only.8,18,44 Individuals in these studies were from several countries, including New Zealand8,25,39 Jordan,16 Israel,12,19 Italy,52 United States,30,33,37,45 India,16,34 Canada,15 United Kingdom,3,29–35 Germany,16–23,35 Australia,38 Taiwan,32 Korea,21 Chad,12 Turkey,14 Slovak Republic,17,36,41 Sweden,31 China,14,52,60 Poland,20 Austria,21,34 Finland and Thailand.31 Study participants were from various ethnic, religious and cultural backgrounds, including Asian Indians or South Asians living in the United States.30 New Zealand8,25 or Canada.15 Buddhists,12,31 and members of the Seventhday Adventist Church.7

Participants in each study adhered to a variety of vegetarian diet types. Table 1 summarizes specific diet characteristics of the studies. Vegetarian categories consisted of semivegetarians (including ‘low meat eaters’ and ’plant-based diet’),7,12,24,35,42 vegetarians,8,9,19,23,30,34,39 ‘non-meat eaters’,25 lacto-vegetarians,11,13,15,18,21,22,26,28,30,33,35,37,38,40,41 ovo-vegetarians,13,22 vegans,8,12,15,16,20,22,23,26,28,33–35,40,43,46 individuals adhering to a macrobiotic diet,8,45,47 and those adhering to raw food diets.10,43 The semivegetarians were defined as individuals consuming no red meat products, but occasionally ingesting white meat (poultry) and fish.7,12 A similar definition was used in a study that included ‘low meat eaters’,35 and among those described as eating a ‘plant-based diet’.42 Two additional studies described their participants as ‘vegetarian’, but included in their sample individuals with consumption of poultry or fish at a frequency of no more than one time per week39 or between one and four times per month.30 The macrobiotic diets were described as one consisting of whole-grain cereal (50–60%), soups (5%), vegetables (20–25%) and beans and sea vegetables (5–10%).44,45,47 Individuals included in one of these diets were reported to consume occasionally small amounts of seafood and little or no dairy or eggs.44 Participants of another study were described as using a very limited amount of products of animal origin.47 Individuals included in another of these studies avoided intake of all animal products including dairy and eggs.45 In addition, one of the studies was based on results obtained from individuals who adhered to the ‘Hallelujah diet’. This diet was described as a pure vegetarian diet using raw fruits and vegetables, nuts, seeds, limited cooked tubers and whole-grain products.10

All studies reviewed included the assessment of vitamin B12 status using serum measurements. Various specific methods of serum vitamin B12 assessment were used, including radio-immunnoassays, immunochemicalimetric methods, microparticle assays, chemiluminescence immunoassays and microbiological assays. Five studies either did not report their specific lab methods or only reported that their serum B12 results were measured using ‘standard’ or ‘validated’ laboratory procedures.12,13,20,26,41

As with a diverse sample of laboratory methods used to evaluate serum B12, the included studies also contained a diverse researcher-defined serum limit that was used to categorize their subjects as vitamin B12 deficient. Most studies defined vitamin B12 deficiency as serum concentration of < 130–150 pmol/l.9,11,12,16,17,19–22,25,37,28,30,34,35,38,40,41,45–48 The lowest defined deficiency was serum concentration below 95 pmol/l.13,52 The highest defined deficiency was defined as serum vitamin B12 < 250 pmol/l.12 In addition, two different units of measurement were used in most studies with regard to serum vitamin B12. Serum concentrations were reported either as pmol/l or pg/ml.

Outcomes

Pregnant women. One study assessed vitamin B12 status in vegetarian pregnant women.47 This study was conducted in Germany and included 27 lacto-ovo-vegetarian participants with a mean age of 30.8 ± 0.9 years. For the first, second and third trimesters, serum B12 deficiency was defined as < 130 pmol/l, < 120 pmol/l and < 100 pmol/l, respectively. Approximately 33% of women in the first trimester of pregnancy were diagnosed as deficient. The deficiency rate for women in the second and third trimesters was 17% and 39%, respectively.27

Infants and toddlers. One study evaluated serum vitamin B12 in infants and toddlers, aged 10.1–20.4 months (n = 47). The rate of vitamin B12 deficiency, defined as serum vitamin B12 < 136 pmol/l, was reported in 45% of these children.47

Children and adolescents. Five of the reviewed studies examined vitamin B12 status in children and adolescents (aged 4–20 years).12,14,22,25,31 Two of these studies included individuals who adhered to a vegan diet.12,31 One of the two vegan studies indicated that there was no incidence of vitamin B12 deficiency among children 8–19 years of age (n = 5) at serum vitamin B12 < 96 pmol/l.12 Among the vegan adolescents (aged 16–20 years, n = 30) included in the other study, 10% had a deficiency, defined as vitamin B12 < 95 pmol/l.13 Deficiency rates of 0%22 and 3.9%14 were reported in two studies that included Chinese children (mean age 5.2 ± 1.5 years, n = 21) and adolescents (aged 4–14 years, n = 51), respectively. These two studies used similar serum vitamin B12 values to define deficiency, < 156 pmol/l22 and < 160 pmol/l, respectively.14 Finally, researchers reported a 33.3% of vitamin B12 deficiency (serum vitamin B12 < 170 pmol/l) in a small sample of migrant Indian girls (n = 6), aged 9–12 years living in New Zealand.25

Adults and elderly. The majority of the reviewed studies assessed B12 deficiency in non-pregnant adults, with ages ranging from 18 to 97 years.47,48 Participants in these studies adhered to a variety of different vegetarian diets.

Vegans: Thirteen studies specifically reported deficiency rates for vegan subjects.12,16,20,23,26,28,29,32,37,43,46 The age of vegan subjects varied from 18 to 84 years. Vitamin B12 deficiency in vegan subjects ranged from 0% to 86.5%.9,12,16,20,23,26,28,29,32,37,43,46 A deficiency rate of 0% (serum vitamin B12 < 142 pmol/l) was reported in one study that included vegan subjects whose diet consisted of vitamin B12-fortified foods. The same study reported vitamin B12 deficiency in 20% of vegan subgroup that did not consume fortified foods. More detailed results of these studies are presented in Table 1. Raw food vegan diets: Donaldson10 reported 12.2% of the sample having serum value < 147 pmol/l and 76% of the sample with serum vitamin B12 < 221 pmol/l. Participants of this study adhered to a Hallelujah diet, of which 85% of ingested foods were raw foods. Rauma et al43 reported a 57% deficiency rate among individuals consuming a ‘living raw food diet’.

Vegetarians (lacto-, ovo- and lacto-ovo-) and vegans combined: Twenty studies reported the prevalence of vitamin B12 deficiency for lacto-vegetarians, ovo-vegetarians, lacto-ovo-vegetarians and vegans as combined samples.8,9,11–13,15,18,19,21–23,29,30,32–34,36,38,40,41 Prevalence of deficiency ranged from 0 to 81%. This prevalence was highly dependent on the definition used by researchers with respect to what value constituted a deficiency.

Macrobiotic diet: Two studies investigated vitamin B12 status in adults adhering to a macrobiotic diet. Both studies were conducted with subjects from the United States and both used a serum vitamin B12 value < 148 pmol/l to define deficiency.
Table 1. Detailed information of reviewed studies

| Reference | Country/ethnicity | Participants | Diet characteristics | Assessment criteria used | Rate of deficiency |
|-----------|------------------|--------------|----------------------|--------------------------|-------------------|
| Majchrzak et al. | Austria | N = 36 vegetarians (10 males and 26 females) Mean age 34.2 ± 13.6 years N = 42 vegans (21 males and 21 females) Mean age 30.7 ± 9.9 years | Vegetarian—no meat, fish, poultry Vegan avoided all products of animal origin Diet duration: 67% at least 5 years 25–31% 1–5 years 2–8% < 1 year | Serum B12 reference value defined according to Sauberlich, normal > 147 pmol/l, deficiency < 110 pmol/l Radioimmunoassay | 0% Vegetarian 2.4% Vegans |
| Lee and Krawinkel | Korea, Buddhists | N = 54 Buddhist nuns Ages 21–44 years | Lacto-vegetarian Diet duration >3 years | Serum B12 deficiency < 150 pmol/l Electrochemiluminescence immunoassay | 1.9% |
| Leung et al. | Chinese | N = 51 children (24 boys and 27 girls) Ages 4–14 years | Lacto-ovo-vegetarian diet (includes dairy, eggs) Diet duration >2 years | Serum B12 normal range 160–625 pmol/l Lab method not reported | 3.9% (N = 2 ‘below normal’) |
| Yen et al. | Chinese | N = 231 vegetarians Mean age = 47 years | Vegetarians defined as eating dairy but no meat or fish Diet duration median 11 years Vegans ate no foods of animal origin Diet duration median 7 years | Serum B12 biochemical deficiency < 118 pmol/l depletion 118–149 pmol/l Quantaphase II radioassay | Vegetarian: 7% deficient; 17% depleted Vegan: 52% deficient; 21% depleted |
| Gilsing et al. | United Kingdom 96% White 4% Bangladeshi or Chinese | N = 232 vegans (all males) Mean age = 47 years | Vegans ate no foods of animal origin Diet duration median 11 years | Serum B12 reference interval 156–674 pmol/l Chemiluminescence immunoassay | Lacto-ovo/lacto-vegans: 6% Vegan: 14% Low meat eaters: 11% |
| Herrmann et al. | Germany | N = 60 (14 males and 46 females) Median age 22 years | Lacto-ovo ate no meat, poultry, fish Lacto—also excluded eggs (lacto-ovo/lacto-veg N = 34) Vegan exclude all foods of animal origin (N = 7) Low meat eaters ate no red meat, but white meat or fish 1–2 x per week (N = 19) Diet duration defined as consistent habits for > 1 year | Serum B12 deficiency < 150 pmol/l Quantaphase II folate radioassay | 12% (N = 3) |
| Larsson and Johansson | Sweden | N = 30 (15 males and 15 females), mean age 17.5 ± 1.0 years | Vegan diet defined as eating food of plan origin Diet duration for least 6 months (and planning to continue) | Adequate blood concentrations of B12 defined as 95–568 pmol/l Quantaphase II B12/folate radioassay | 10% (N = 3) |
| Haddad et al. | United States | N = 25 (10 males and 15 females) Mean age 20.5 ± 2.5 years | Vegans defined as excluding meat, fish, poultry, dairy products, eggs Diet duration mean 4.2 years Adherence to Hallelujah diet defined as pure vegetarian, with raw veg, fruit, raw nuts and seeds, limited cooked tubers and whole-grain products Diet duration mean 39 months | Serum B12 deficiency < 150 pmol/l Quantaphase II radioassay | 12.2% 2 Men (11.7%) 4 Women(12.5%) |
| Donaldson | USA | N = 49 (17 males and 32 females) Average age 55 ± 9 years | Vegan diet Diet duration 5–35 years | Serum B12 deficiency < 150 pmol/l Quantaphase II radioassay | 12.2% |
| Bar-Sella et al. | Israel | N = 36 (males and females) Age 18–19 years: N = 5 Age 20–39 years: N = 5 Age 40–59 years: N = 13 Age 60–79 years: N = 13 30.5% Borderline (N = 11) | Vegan diet Diet duration 5 months | Serum B12 deficiency < 130 pg/ml Borderline 130–200 pg/ml Radioimmunoassay | 13.9% Deficient (N = 5) |
| Vegetarian diet described as plant-based, eat very few dairy foods, rarely eat meat, occasionally consume poultry and eggs Diet duration not reported | | | Serum B12 lower limit of normal defined as ≤ 140 pmol/l Chemiluminescence | Ingenbleek and McCully | Africa (Chad) N = 24 (rural males Ages 18–30) |
| Lowik et al. | Netherlands; Caucasian | N = 40 (17 males and 23 females) Mean age: | Lacto-ovo-vegetarian ate no meat, fish, poultry Lacto-vegetarians also excluded eggs Diet duration described as '32 | Serum B12 deficiency < 138 pmol/l Lab method not available | 22.5% 6 Men (35.3%) 3 Women (13.0%) |
| Reference                           | Country/ethnicity               | Participants                                                                 | Diet characteristics                                                                 | Assessment criteria used                                                                 | Rate of deficiency |
|------------------------------------|--------------------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------|
| Gammon et al.                      | South Asians living in New Zealand (India, Pakistan, Sri Lanka, Fiji, other) | Men—82.8 years, Women—81.1 years N = 34 females Mean age 36 ± 10.1 years (subjects) had been vegetarian for more than 45 years' Vegetarian defined as absence of meat in diet Diet duration not reported | Serum B12 deficiency < 150 pmol/l Marginal B12 status 150–221 pmol/l Radioassay          | 23.5% Deficient 35% Marginal status                                                   |
| Herrmann et al.                    | Germany and Netherlands        | N = 66 vegetarians Median age 48 years N = 29 vegans Median age 37 years Males and females Lacto-ovo—excluded meat, poultry, fish Lacto—excluded exclude meat, poultry, fish, egg Vegan excluded all foods of animal origin | Low serum B12 concentration < 156 pmol/l Chemiluminescence immunoassay                   | 26% Vegetarians 52% Vegans                                                            |
| Koebnick et al.                    | Slovak Republic                | N = 62 vegetarians (24 males and 38 females) N = 32 vegans (10 males and 22 females) Mean age 41.5 ± 1.8 years Diet duration ≥ 1 year | Serum B12 deficiency < 179.0 pmol/l Elecsys 2010 immunoassay                          | 26% Vegetarians 78% Vegans                                                            |
| Karabudak et al.                   | Turkey                         | N = 26 (all females) Mean age 29.0 ± 8.84 years Diet duration mean 10.5 ± 6.77 years Strict vegan defined as 'pure vegan diet' Moderate vegan—ate maximum of 5% of total energy from eggs and/or dairy products Diet duration: Strict vegan mean 7.14 ± 6.69 years Moderate vegans mean 4.69 ± 2.97 years | Serum B12 deficiency ≤ 150 pmol/l (also assessed at ≤ 156 pmol/l) Chemiluminescence competitive binding assay | 26.9%* results combined all vegetarian types |
| Waldmann et al.                    | Germany                        | N = 86 strict vegans (48.8% males and 51.2% females) Mean age 43.8 ± 15.6 years N = 45 moderate vegans (35.6% males and 64.4% females) Mean age 44.6 ± 15.0 years | Serum B12 deficiency < 110 pmol/l (52% ≤ 156 pmol/l) Chemiluminescence 65.5% ≤ 156 pmol/l Moderate vegans (37.8% ≤ 156 pmol/l) | 28.2% All vegans 39.5% Strict vegans 66.7% Moderate vegans                           |
| Krajcovicova-Kudlackova et al.     | Slovak Republic                | N = 52 (all females) Mean age 25.2 ± 0.4 years Diet duration mean 9.7 ± 0.5 years Lacto-vegetarian consumed < 240 ml milk per day Lacto-ovo- and veg and lacto-ovo- and veg and lacto-ovo- and veg and lacto-ovo- and veg Moderate vegans and meat and meat products Diet duration at least 3 years | Serum B12 deficiency < 179 pmol/l Elecsys immunoassay (Roche test)                     | 31% N = 14                                                                |
| Hung et al.                        | Taiwan, Buddhists              | N = 45 (39 lacto-vegetarians and 6 vegans) (all females) Mean age 30.8 ± 0.9 years Diet duration avg. 7.9 years Moderately vegetarians defined as completely omit meat and meat products Diet duration at least 3 years | Serum B12 deficiency < 179.8 pmol/l Microparticle enzyme immunoassay                   | 31% N = 14                                                                |
| Koebnick et al.                    | Germany                        | N = 27 (pregnant women) Mean age 30.8 ± 0.9 years Diet duration ≤ 3 years Ovo-lacto-vegetarian defined as completely omit meat and meat products Diet duration at least 3 years | Serum B12 < 130 pmol/l (1st tri); < 120 pmol/l (2nd tri); < 100 pmol/l (3rd tri) IMX cobalamin assay (microparticle) | 33% First tri 17% Second tri 39% Third tri (all % extrapolated from graph—Figure 1) |
| Alexander et al.                   | New Zealand                    | N = 18 (13 vegetarians and 5 vegans; males and females) N = 12 (8 males and 4 females) Females—Vegetarian Mean age 26 years Vegan mean age 30y Males—Vegetarian Mean age 28 years | Serum B12 reference range 150–680 pmol/l SimulTRAC radioassay kit (Becton Dickson)      | 33.3% N = 6                                                                |
| Rush et al.                        | Migrant Indian girls, living in Auckland, New Zealand | N = 6 (all girls) Ages 9–11 years Diet duration described by mothers as ‘practised for many generations in their family’ Diet duration not reported | Serum B12 deficiency < 170 pmol/l Lab methods not available                           | 33.3%                                                             |
| Carmel et al.                      | Asian-Indian individuals living in United States | N = 8 (6 males and 2 females) Ages 26–36 years Not defined, but group consisted of ovo-lacto-vegetarians, lacto-vegetarian and vegans Some vegetarians reported eating poultry and fish 1–4 x per month Diet duration not reported | Serum B12 normal range 180–600 pmol/l Quantaphase II radioisotope dilution | 37.5% N = 3                                                                |
| Dagnelle et al.                    | Netherlands                    | N = 47 (males and females) Mean age 15.2 months (10.1–20.4 months) Diet described by researchers as consisting of grain cereals (mainly rice), vegetables, pulses (mainly soy), and sea vegetables and only very Diet duration not reported | Serum B12 < 136 pmol/l Competitive protein-binding assay                               | 45%                                                         |
| Reference          | Country/ethnicity            | Participants | Diet characteristics                                                                 | Assessment criteria used                                                                 | Rate of deficiency |
|--------------------|------------------------------|--------------|---------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|-------------------|
| Miller et al.      | United States               | N = 110 (46 males and 64 females) | Median age 33 years (21–70)  
Macrobiotic diet defined as typically consisting of 50–60% whole cereal grains, 5% soups, 20–25% vegetables and 5–10% beans and sea vegetables; occasional small amounts seafood eaten, but no meat and little or no dairy or eggs  
Diet duration median 25 years | Low vitamin B12 concentrations < 148 pmol/l  
Radioimmunoassay | 51% |
| Woo et al.         | Chinese (elderly)           | N = 106 (all females) | Mean age 81.3 ± 7.6 years  
Vegetarian not specifically defined but included both vegans and lacto-ovo-veg | Serum B12 deficiency < 150 pmol/l  
Measured ‘using standard laboratory methods’  
Radioimmunoassay | 53.8% (N = 57) |
| Specker et al.     | United States               | N = 17 (all females) | Mean age 31 years (22–40)  
Vegetarians described as practicing a macrobiotic diet—50–60% whole cereal grains, 5% soups, 20–25% vegetables, 5–10% beans and sea vegetables; avoid animal products; no dairy products or eggs  
Diet duration median 72 months (14–137 months) | Low serum B12 < 148 pmol/l  
Radioimmunoassay | 56% |
| Rauma et al.       | Finland                      | N = 21 (20 females and 1 male) | Females mean age 47 years (27–69)  
Male age 40 years  
Uncooked vegan diet (‘living food diet’) with most food items fermented or sprouted, thought to enhance growth of vitamin-B12-producing bacteria  
Diet duration average 5.2 years (0.7–14) | Serum B12 lower reference limit 200 pmol/l  
Dual radioassay | 57% |
| Waldmann et al.    | Germany                      | N = 98 strict vegans (49% males and 51% females) | Mean age 43.4 ± 15.4 years  
N = 56 moderate vegans (33.9% males and 66.1% females)  
Mean age 45.7 ± 14.2 years  
Moderate vegan—aeti < 5% of ingested energy from eggs, milk and dairy  
Diet duration: Strict vegan mean 7.70 ± 6.40 years  
Moderate vegan mean 5.06 ± 4.03 years | Serum B12 deficiency defined as < 150 pmol/l  
(also assessed deficiency at < 250 pmol/l)  
Chemiluminescence | 58.3% Strict vegans  
(86.5% < 250 pmol/l)  
34.5% Moderate vegans  
(69.1% < 250 pmol/l) |
| Refsum et al.      | Asian Indians                | N = 78 (males and females) | Ages 27–55 years  
Subjects considered vegetarian if never ate mutton, poultry, fish or eggs  
Diet duration not reported | Serum B12 deficiency < 150 pmol/l  
Microbiological assay | 60% |
| Gupta et al.       | South Asians (India, Pakistan) living in Toronto | N = 172 (70 males and 102 females) | Ages 18–84 years (avg age 42 years)  
Vegetarian classification included vegans, lacto- and lacto-ovo-vegetarians  
Diet duration not reported | Serum B12 deficiency < 132 pmol/l  
Microparticle intrinsic factor assays (three types) | 66.3% |
| Yajnik et al.      | India                        | N = 137 males (41% rural, 11% slum, 44% urban) |  
Lacto-vegetarian  
Diet duration not reported | Serum B12 low concentration < 150 pmol/l  
Radioimmunoassay | 68% Rural  
51% Slum  
81% Urban middle-class |
| Between 150 and 221 pg/ml or 200–300 pmol/l |  |  |  |  |  |
| Madry et al.       | Poland                       | N = 20 (6 males and 14 females) | Median age = 23 years  
Subjects agreed to switch to vegan diet for 5 years  
N = 10 strict vegan  
N = 10 vegans with B12-fortified foods  
Diet duration 5 years | Serum B12 considered abnormal < 193 pg/ml  
Chemiluminescence immunoassay | 20% Strict vegans  
0% Vegan with B12-fortified foods |
| Morad et al.       | Israel, individuals with intellectual disability | N = 47 (25 males and 22 females) | Ages 19–61+ years  
‘Vegetarian’ not defined  
Diet duration not reported | Serum B12 deficiency < 157 pg/ml  
Lab method not reported, used Clalit Health Service Laboratory | 25.5% |
| Bissoli et al.     | Italy                        | N = 31 vegan (19 males and 12 females) | Mean age 45.8 ± 15.8 years  
N = 14 lacto-ovo-vegetarians  
Vegan avoided all animal products  
Lacto-ovo-vegetarian consumed milk and eggs, but not meat  
Diet duration at least 5 years | Very low serum B12:  
47.8% vegan  
33.3% Lacto-ovo-vegetarians |  |
Fifty-one percent (n = 110) and 56% (n = 17) of subjects, respectively, were found to be deficient.14,46

Semivegetarians: Five studies reported deficiency rates for a sample that included participants who consumed vegetarian and semivegetarian diets.17,24,35,39,42 Deficiency rates in these five studies ranged from 8%35 to 33.3%.39 Study-specific deficiency criteria ranged from 7 to 81% using different definitions for semivegetarian diets.17,24,35,39,42 Deficiency rates for male semivegetarians clearly were found to be dietary deficiency. It needs to be pointed out, however, that even among vegans who consumed vitamin B12-fortified foods, the research-ers documented a steady decline in serum vitamin B12 over a 5-year period of study duration. This finding indicates that in long-term prevention of vitamin B12 deficiency, higher doses of vitamin B12 than the dose currently used in some fortified foods may be needed. This may especially be true for older adults and the elderly owing to age-related decline in absorption rate. Additional studies are needed to support or refute this conclusion. These findings indicate that including vitamin B12 supplements even when foods fortified with vitamin B12 are ingested is the most effective way of preventing deficiency.44

Gender-specific deficiency rates (non-pregnant adults)

Some of the authors specifically looked at subjects of one sex8,9,17,18,21,24,33,40–42,45 or reported their results by separating deficiency rates for male and female subjects.10,11,15 Some of the highest deficiency rates across all studies reviewed were reported in lacto-vegetarian, urban, middle-class Indian male subjects (81%)18 and in adult American female subjects (56%) who consumed a macrobiotic diet.45 Overall, deficiency rates for female subjects ranged from 1.9 to 56% with deficiency definitions ranging from < 147.8 to < 220 pmol/l. Deficiency rates for male subjects ranged from 7 to 81% using deficiency definition from < 118 to < 150 pmol/l. In the studies that reported results comparing male and female subjects, no considerable differences were noted between the two sexes.10,13,11,15

**DISCUSSION**

This review assessed vitamin B12 deficiency prevalence among individuals adhering to vegetarian diets. A comparison of deficiency prevalence between studies is not easy considering the wide range of serum vitamin B12 values defined by study authors as indicative of vitamin B12 deficiency. According to the Institute of Medicine, a serum of 120–180 pmol/l is indicative of deficiency. Most of the studies in this review defined vitamin B12 deficiency in this range.2

Of the four studies that assessed vitamin B12 deficiency at higher serum values, two reported results specifically for adult vegans. Reported results found 47.8% deficiency among vegans (< 220 pmol/l)32 and 86.5 and 69.1% (< 250 pmol/l) in ‘strict’ and ‘moderate’ vegans, respectively.26 These results suggest that the prevalence of vitamin B12 deficiency among vegans is especially high even when their vitamin B12 status is assessed using a relatively high serum vitamin B12 value. The fact that a higher prevalence of deficiency is found among ‘strict’ vegans clearly indicates the importance of consuming foods containing vitamin B12 or using vitamin B12 supplements.

Deficiency prevalence of 0% was reported among vegans who consumed vitamin B12-fortified foods.25 Although these findings can be in part explained by a relatively lenient deficiency definition (< 142 pmol/l), vitamin B12 provided by fortification undoubtedly was a factor in preventing the occurrence of a deficiency. It needs to be pointed out, however, that even among participants consuming vitamin B12-fortified foods, the research-ers documented a steady decline in serum vitamin B12 over a 5-year period of study duration. This finding indicates that in long-term prevention of vitamin B12 deficiency, higher doses of vitamin B12 than the dose currently used in some fortified foods may be needed. This may especially be true for older adults and the elderly owing to age-related decline in absorption rate. Additional studies are needed to support or refute this conclusion. These findings indicate that including vitamin B12 supplements even when foods fortified with vitamin B12 are ingested is the most effective way of preventing deficiency.44
The study led by Madry et al. is of particular importance for another reason. In the past, it was widely believed that it took a very long time for vitamin B12 deficiency to develop when foods that are a natural source of this vitamin are not ingested. In their study, Madry et al. included participants who switched from consuming an omnivorous to a vegan diet for a period of 5 years. The results showed a progressive decline in the mean serum vitamin B12, with two participants (20%) among those who did not consume vitamin B12-fortified foods being diagnosed with vitamin B12 deficiency (<193 pg/ml) within the study period. This prevalence would likely be higher if in addition to serum vitamin B12, other biomarker methods believed to be more accurate, such as methylmalonic acid, were used.

Vitamin B12 deficiency seems to be higher among vegetarians from India and Pakistan compared with those living in other regions. Gupta et al. reported a deficiency prevalence among individuals of Indian and Pakistani origin living in Canada. In this retrospective study, Gupta et al. found 66.3% deficiency (defined as serum vitamin B12 <132 pmol/l) of their sample having vitamin B12 deficiency. Similarly, Yajnik et al. reported deficiency rates of 81, 68, and 51%, among Indian men with different socioeconomic status. Men from urban, middle-class had notably higher rates of deficiency compared with both men from rural and slum socioeconomic class. Yajnik et al. also suggested that the higher deficiency prevalence in the male subjects from the middle-class may be reflective of ingestion of less microbial B12 from contaminated food and water sources. Although other studies confirmed that the contamination of water and unwashed products may contain B12, the high deficiency prevalence among individuals included in this study indicates that vegetarians cannot rely on them as means of vitamin B12 deficiency prevention.

The deficiency prevalence among pregnant women differed depending on which trimester the women were in. Even though serum vitamin B12 indicative of a deficiency among women in the last trimester was lower compared with the criteria in the first two trimesters (<100 pmol/l, compared with <120 and <130 pmol/l, in the first and the second trimesters, respectively), women in the third trimester were found to have a higher prevalence of deficiency (39% vs 33% and 17% for the first and second trimesters, respectively). Although the lower serum vitamin B12 during pregnancy may be in part explained by expanded blood volume, this dilution effect is unlikely the reason for the higher prevalence of deficiency among women in the last trimester. Blood volume peaks at about the 34th to 36th week of gestation and remains unchanged until term. It is more likely that the higher deficiency prevalence among pregnant vegetarian women in the third trimester is indicative of depleted vitamin B12 stores rather than expanded blood volume. Pregnant women have higher needs for vitamin B12. The low vitamin B12 status of pregnant vegetarian/vegan women may result in diagnoses of vitamin B12 deficiency in infants. Such deficiency is often associated with severe symptoms, including failure to thrive, inability to accept solid foods, stunting and developmental delays. This is why ensuring that a reliable source of vitamin B12 (e.g. vitamin B12 supplement) during pregnancy is of the most critical importance.

The findings of the review show that individuals who follow a vegan diet, and do not take vitamin B12 supplements nor eat foods fortified with this vitamin, have higher prevalence of a deficiency compared with those adhering to other types of vegetarian diets. Similarly, ‘strict’ vegans were found to have a higher prevalence of deficiency when compared with ‘moderate’ vegans. In fact, every study that reported the prevalence of deficiency for vegans separately from other vegetarians showed higher prevalence of deficiency among vegans. Nevertheless, the findings also suggest that, with few exceptions, there is also a relatively high prevalence of deficiency among individuals who follow all other types of vegetarian diets. Thus, vegetarians, and especially vegans, should strongly consider using vitamin B12 supplements to ensure adequate vitamin B12 intake, and to help prevent deficiency.

CONCLUSION

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