



A study of the prevalence of vitamin B12 deficiency in Turlock, California

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B12 (cobalamin) is essential to maintain proper neurologic functioning. Patients with vitamin B12 deficiency may suffer from fatigue, neurologic disease, paresthesia, and megaloblastic anemia. Overall, the prevalence of B12 deficiency is difficult to assess because there is no consistent diagnostic criteria by which practitioners can distinguish deficient from nondeficient patients. In developed countries, it is estimated that 20% of the population is cobalamin-deficient, with other studies suggesting numbers varying between 5% and 60%. The goal of this community-based case-control study was to investigate the prevalence of B12 deficiency in a developed population and to evaluate and discuss factors thought to contribute to B12 deficiency. A computer record search found the number of B12-deficient patients diagnosed at three different primary care offices in the city of Turlock, California. These search results were further analyzed for the collective prevalence of B12 deficiency, as well as the age-based and gender-based prevalence. Results show an overall B12 deficiency prevalence of 8.78%. Age-based results show the highest prevalence of B12 deficiency within the 61 to 80 years-old patient group compared with the 21 to 40 years-old and 41 to 60 years-old age groups. Gender-based results show an approximate 2:1 ratio difference when B12-deficient females were compared with B12-deficient males. This study aims to expand epidemiologic knowledge and clinical awareness of cobalamin deficiency to improve patient care and quality of life.

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Vitamin B12 (cobalamin) is necessary to maintain proper neurologic functioning. Cobalamin can be found in high amounts in red meat and seafood and in lesser amounts in chicken, eggs, and dairy products.^{1,2} The body can store vitamin B12 in the liver and delay symptoms of deficiency from three to ten years in persons with inadequate intake of cobalamin.^{2,3} Patients with vitamin B12 deficiency can have

fatigue, neurologic disease, paresthesia, and megaloblastic anemia. Patients may also develop Hunter's glossitis, a condition in which the tongue takes on a smooth and shiny appearance caused by atrophy of the surface papillae.¹⁻⁵

In developed countries, it is estimated that approximately 20% of the population is cobalamin-deficient, although studies vary between 5% and 60% owing to the lack of a standard definition of B12 deficiency.⁶ Some people may fall within a normal laboratory diagnostic range of vitamin B12 and still have symptoms of deficiency, whereas other people might be diagnostically vitamin B12-deficient ac-

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cording to laboratory results but not have any symptoms.^{5,7-9} This makes standardizing diagnostic criteria very difficult. Proof that symptoms of vitamin B12 deficiency are indeed caused by deficiency of the vitamin is exemplified through administration of vitamin B12 and the reversal of symptoms.⁷ In the past, this type of therapeutic testing was the primary method to confirm diagnosis of cobalamin deficiency. Today, therapeutic testing is used as an adjunct to the current diagnostic method of measuring vitamin B12 blood serum levels.⁸

Causes of B12 deficiency

Inadequate intake of cobalamin is a major cause of vitamin B12 deficiency.¹⁻⁴ The recommended intake varies with body size and type because some people require more vitamin B12 than others to prevent neurological symptoms. Therefore, an exact adequate value is unknown to prevent all symptoms of B12 deficiency, although diets that contain at least 0.5 µg/day prevent megaloblastic anemia.^{1,2,4} In addition, babies born to or breast-fed by mothers who are vitamin B12-deficient will also receive inadequate intake of the vitamin.^{1,2,10}

Vitamin B12 deficiency can be caused by malabsorption due to conditions such as pernicious anemia, certain enzyme deficiencies, and damage or resection of the terminal ileum.¹⁻⁴ Pernicious anemia is an autoimmune disorder caused by antibodies reacting against intrinsic factor (a factor needed to bind and absorb cobalamin) and/or autoimmune destruction of gastric mucosa.^{1-3,7} Several pancreatic enzymes are needed to help transport cobalamin through the stomach to the small intestine. People with certain enzyme deficiencies thus have difficulty with vitamin B12 absorption. Furthermore, the ileum is needed to convert cobalamin into a form that can be delivered through the body. Diseases such as Crohn’s disease, amyloidosis, scleroderma, tuberculosis, and certain lymphomas can cause damage to the terminal ileum.¹⁻³

Food-cobalamin malabsorption syndrome commonly caused by gastric atrophy is a frequent reason for deficiency in the elderly but occurs in other populations as well.^{5,11-13} This condition results from by the inability of the body to separate cobalamin from food or transport proteins throughout the body.^{1,5} *Helicobacter pylori* infection contributes to gastric atrophy, as does chronic alcoholism and the use of certain medications such as antibiotics, biguanides, and antacids.^{1-4,14}

Malabsorption of cobalamin can also be attributed to parasitic infection from the fish tapeworm *Diphyllobothrium latum*, which absorbs cobalamin from the small intestine. The protozoan *Giardia lamblia* has also been linked to decreased B12 absorption, although this is not as well documented as tapeworm-based deficiency.⁴ Infestations are most common in areas where there is consumption of raw fish or contaminated drinking water. A large, long-standing

infestation of the aforementioned tapeworm or chronic infection with *Giardia* is needed to cause significant malabsorption of vitamin B12.¹⁻⁴

Contributing factors to B12 deficiency

Age

Research has long shown that elderly populations in the United States and Europe have a higher prevalence of cobalamin deficiency compared with younger populations,^{1-9,11-13,15} with a minority of studies in dispute.¹⁶ As an example, Mollin and Ross noted in their 1952 study that people older than 70 years had lower serum cobalamin than both 15 to 40 years-old and 50 to 70 years-old groups.¹⁵ The high prevalence of cobalamin deficiency among the elderly is likely caused by the higher incidence of pernicious anemia in this group, although this is currently thought to be a small contributor overall compared with absorption problems such as food-cobalamin malabsorption syndrome.^{4,7,17} Elderly Latinos in the United States especially were shown to have a high prevalence of low B12 serum levels when compared with elderly Caucasians, African Americans, and Asian Americans.⁴

Diet

Although many people follow a vegetarian or vegan diet because of religious, cultural, or health reasons, they are putting themselves at risk for vitamin B12 deficiency, because meat is a primary source for the vitamin.^{1-4,18,19} In Hong Kong, a study showed that 75% of elderly vegetarians had vitamin B12 deficiency.⁴ In India, the majority of the population is lacto-vegetarian (consumption of dairy products in addition to a plant-based diet), making megaloblastic anemia and neurologic symptoms highly prevalent among the Indian community.¹⁸ One study showed that 11% of young infants in India suffered from tremor because of inadequate vitamin B12 levels.²⁰ Populations in the Middle East and rural Central Mexico also consume less meat in their diets and consequently show an increased prevalence of B12 deficiency.⁴

Table 1 Office 1: Patient comparison between vitamin B12-deficient patients and non-vitamin B12-deficient patients

	Male patients	Female patients	Total patients
B12-deficient	66	225	291
Not B12-deficient	440	825	1265
	506	1050	1556

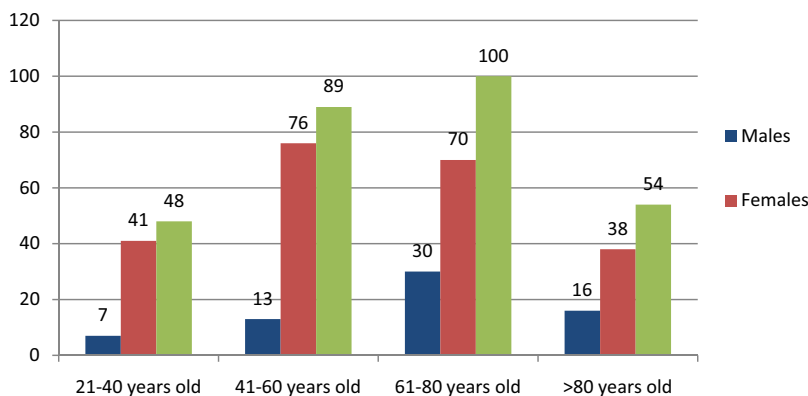


Figure 1 Office 1: Patients with vitamin B12 deficiency.

Gender

The contribution of gender to cobalamin deficiency appears to be controversial. A study of 88 male and 89 female multi-ethnic college students found no overall difference in cobalamin intake or serum levels,²¹ whereas another study of 159 healthy subjects found higher serum levels in females compared with males.²² Females have a higher prevalence of pernicious anemia–based cobalamin deficiency compared with males, particularly in Northern Europe and the United States.^{1,4} In a study of seniors in California, there were 8300 females per 100,000 with pernicious anemia and only 4100 males per 100,000 with pernicious anemia; and in Minnesota there was an incidence of 49.2 females and 25.1 males with pernicious anemia.⁴

Prevalence of B12 deficiency in Turlock, California

Methods

Demographic reports on Turlock, California were studied using information from the US Census Bureau. Data

were collected from three primary care offices in Turlock, California, with diverse patient populations that reflect the population of that city. Reports were developed using a computer-based medical record search for patients with vitamin B12 deficiency as a diagnosis in each of the three primary care offices. All three offices used the following diagnostic criteria for vitamin B12 deficiency: (1) serum cobalamin level <200 pg/mL with or without additional findings or (2) serum cobalamin level 200 to 400 pg/mL with additional findings such as clinical symptoms, hematologic changes, and/or high suspicion based on risk factors (e.g., age, diet, race). Cases meeting the second criterion were often confirmed by resolution of symptoms/hematologic changes upon replacement therapy of B12. The number of vitamin B12–deficient patients found in each practice was then compared with the total number of patients without B12 deficiency as a diagnosis within that same practice. Data were then combined from the three practices to obtain an overall picture of the prevalence of vitamin B12 deficiency in Turlock, California. Furthermore, data were separated to develop a better idea of which (1) age range and (2) gender is most affected by vitamin B12 deficiency. This study reflects a community-based case-control study where cases of vitamin B12 deficiency patients were compared with the control group of non–vitamin B12–deficient patients in the community of Turlock.

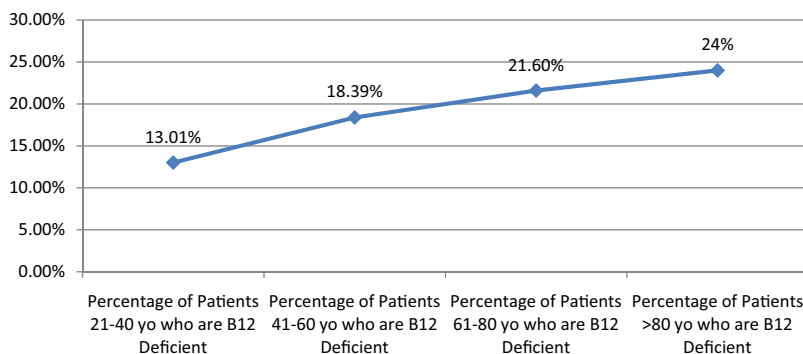


Figure 2 Office 1: Percentage of B12-deficient patients per age group relative to amount of patients per age group. Data were calculated by dividing the total number of B12-deficient patients in each age group by the total number of patients of the same age group.

Table 2 Office 2: Patient comparison between vitamin B12-deficient patients and non-vitamin B12-deficient patients

	Male patients	Female patients	Total patients
B12-deficient	32	41	73
Not B12-deficient	659	793	1452
	691	834	1525

Results

Office 1

Table 1 shows there are 291 (18.7%) B12-deficient patients of 1556 total patients in the practice. The greatest absolute number of B12-deficient patients is in the 61 to 80 years-old range (Figure 1). However, when comparing the amount of B12-deficient patients in an age range to the total amount of patients in the same age range, data show an upward trend in percentage of B12-deficient patients with increasing age (Figure 2). Although only 54 of the total 291 B12-deficient patients were in the >80 years-old category, data show that these patients accounted for 24% of total patients >80 years-old in Office 1. When comparing the absolute number of B12-deficient men and women separately, there are more women in each age range than men (Figure 1). In total, there are approximately twice as many female patients than male patients who are seen in Office 1, but there are more than twice as many female B12-deficient patients than male B12-deficient patients in every age category (Figure 1). Furthermore, Table 1 illustrates that there are 66 (13.04%) male cobalamin-deficient patients of 506 total males and 225 (21.43%) female cobalamin-deficient patients of 1050 total females.

Office 2

Table 2 shows there are 73 (4.79%) B12-deficient patients of 1525 total patients in the practice. As in Office 1, the greatest absolute number of B12-deficient patients is in

the 61 to 80 years-old range (Figure 3). When comparing the amount of B12-deficient patients in an age range with the total amount of patients in the same age range, data show an upward trend in percentage of B12-deficient patients with increasing age, also similar to Office 1 (Figure 4). Only 13 of the 73 B12-deficient patients were in the >80 years-old category, but data show that these patients account for 12.15% of total patients >80 years-old in Office 2. When comparing the absolute number of B12-deficient men and women separately, there are equal amounts of B12-deficient men and women in the <21 years-old and 21 to 40 years-old categories, more B12-deficient men than women in the 41 to 60 years-old categories, and more B12-deficient women than men in the 61 to 80 years-old and >80 years-old categories (Figure 3). There were approximately 140 more female patients than male patients seen in Office 2 and more female B12-deficient patients than male B12-deficient patients. Table 2 illustrates that there are 32 (4.63%) male B12-deficient patients of 691 total males and 41 (4.92%) female B12-deficient patients of 834 total females.

Office 3

Table 3 shows there are 11 (0.93%) B12-deficient patients of 1188 total patients in the practice. The greatest absolute number of B12-deficient patients is in the 61 to 80 years-old range (Figure 5), as in Offices 1 and 2. Also similar to Offices 1 and 2, when comparing the amount of B12-deficient patients in an age range with the total amount of patients in the same age range, data show an upward trend in percentage of B12-deficient patients with increasing age (Figure 6). In contrast to Offices 1 and 2, Office 3 had no B12-deficient patients under the age of 40. Although three of the total 11 cobalamin-deficient patients were in the >80 years-old range, data show that these patients account for 2.70% of total patients >80 years-old in Office 3, slightly more compared with other age ranges (Figure 6). When comparing the absolute number of B12-deficient men and women separately, there were more B12-deficient women than men in the 41 to 60 years-old and 61 to 80 years-old categories, and equal amounts of men and women in the >80 years-old category (Figure 5). There were approximately 70 more female than male patients seen in

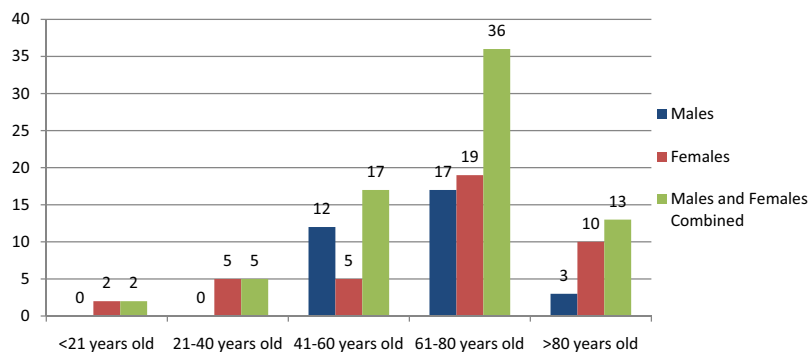


Figure 3 Office 2: Patients with vitamin B12 deficiency.

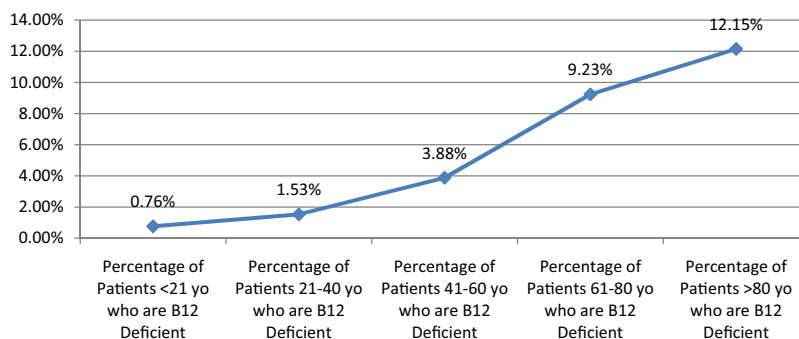


Figure 4 Office 2: Percentage of B12-deficient patients per age group relative to amount of patients per age group. Data were calculated by dividing the total number of B12-deficient patients in each age group by the total number of patients of the same age group.

Office 3 and more female than male B12-deficient patients. Table 3 shows that there were three (0.54%) male cobalamin-deficient patients of 552 total males and eight (1.26%) female cobalamin-deficient patients of 636 total females.

Combined data

There are 375 (8.78%) B12-deficient patients of 4269 patients in this study. The greatest absolute number of B12-deficient patients were in the 61 to 80 years-old range, but the greatest percentage of B12-deficient patients per age group was in the >80 years-old category. There are also 274 (10.87%) B12-deficient women of 2520 female patients and 101 (5.77%) B12-deficient men of 1749 male patients, giving an approximate ratio of 2:1 female-to-male B12-deficient patients.

Discussion

The population size of Turlock, California is 67,866, with 17,432 people who are foreign-born; approximately 50.2% of the population is female and 49.8% is male.²³ The population breakdown is White (72.3%), and a mix of different ethnicities (27.7%). The Asian population makes up 4.5% with more than half comprising Asian Indians.²⁴ The Latino/Hispanic demographic, which includes any race (Whites and Non-White) declaring themselves as such, makes up 34.4% of the Turlock population, which is more than double the US average of 15.1%.²³

Because Turlock has a significant percentage of people who are from Latin, Asian, and Indian backgrounds, it is expected that there should be a high prevalence of vitamin B12-deficient individuals. As noted earlier, elderly Latinos have a high prevalence of low vitamin B12 levels, as do certain Asian and Indian groups, who primarily consume diets low in meat.^{4,18} However, only 8.78% of the studied Turlock population is cobalamin-deficient, which is lower than the 20% average in developed countries.¹⁷ Possible factors to explain this discrepancy are detailed next.

Results of vitamin B12 deficiency by age group are consistent with previous studies.^{1-9,11-13,15} A greater percentage of elderly patients in this study are vitamin B12-deficient compared with the younger population. When considering gender, the results of this study showed a 2:1 ratio of female to male B12-deficient patients. The higher prevalence of pernicious anemia in women might partially explain why there are more women in Turlock that are vitamin B12-deficient, but more research needs to be done to evaluate the prevalence of pernicious anemia and determine whether it is a true contributing factor.^{1,4} Further studies also need to investigate other confounding factors, such as the possibility that more women than men in Turlock are vegetarians or vegans.^{1-4,18-20}

As described earlier, major problems with investigating B12 deficiency is the lack of standardized diagnosis guidelines, and the fact that patients display symptoms at differing levels of serum cobalamin.^{5,7-9} The latter issue was exemplified by a patient seen in Office 1. An 81-year-old female patient with serum cobalamin <50 pmol/L (below the detectable amount) presented with classic Hunter’s glossitis and macrocytosis, but no overt neurological symptoms or fatigue. Inadequate dietary intake of cobalamin and malabsorption caused by alcoholism were ruled out through patient history. The patient was subsequently tested for *H. pylori* infection and was found to be negative. In this study, her age and gender place her in the groups with the highest prevalence for B12 deficiency. Further studies could be done in the future to determine the exact cause of this patient’s B12 deficiency. Perhaps this patient was one of many elderly who have food-cobalamin malabsorption syndrome.^{5,11-13}

Table 3 Office 3: Patient comparison between vitamin B12-deficient patients and non-vitamin B12-deficient patients

	Male patients	Female patients	Total patients
B12-deficient	3	8	11
Not B12-deficient	549	628	1177
	552	636	1188

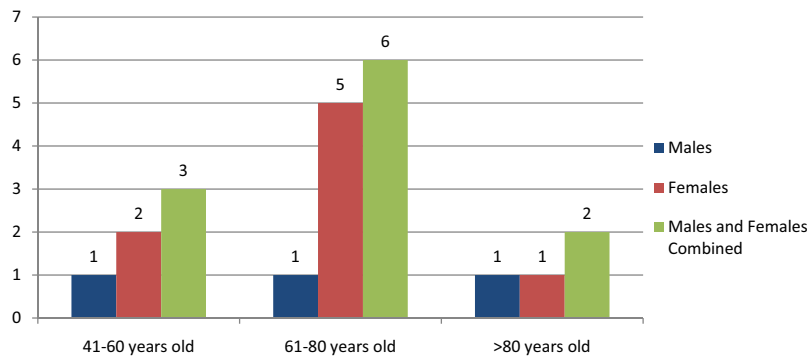


Figure 5 Office 3: Patients with vitamin B12 deficiency.

This study may be skewed by information bias owing to misclassification of which patients are truly deemed vitamin B12-deficient. A current problem with cobalamin deficiency diagnosis and treatment is the lack of a gold standard for defining vitamin B12 deficiency among different patient populations.²⁵ As a result, doctors may draw the cutoff for vitamin B12 deficiency differently from office to office or even from patient to patient, making accurate classifications difficult. In addition, doctors may screen for vitamin B12 levels at different frequencies. For instance, the offices in this study used similar diagnostic criteria, but through observation, Office 1 frequently ordered vitamin B12 levels when ordering laboratory work, regardless of whether patients had symptoms of B12 deficiency, whereas Office 3 only ordered vitamin B12 levels when patients demonstrated symptoms suggestive of B12 deficiency. Therefore, more B12-deficient patients may have been discovered in Office 1 compared with Office 3 based on screening frequency, despite both offices using similar criteria for making the final diagnosis.

Confounding bias may also be present in this study. Although groups were studied separately by age and gender, confounding factors of race, socioeconomic status, and health insurance coverage were unable to be studied individually. Some groups of people may not receive health screening as frequently because of some or all of these factors. Thus, it is unclear how strongly race, socioeconomic status, and health insurance coverage contributed to the results. More detailed research and analysis is needed to rule out such confounding factors.

Conclusion

This study assessed the prevalence of vitamin B12 deficiency in Turlock, California and found that elderly patients had a higher prevalence of B12 deficiency than younger patients, and women also had a higher prevalence of B12 deficiency than men. The increased prevalence of B12 deficiency found among elderly patients is consistent with previous studies and is likely attributed to atrophic gastritis and food-cobalamin malabsorption syndrome.^{5,11-13} The higher prevalence of cobalamin deficiency found in female patients in Turlock, California is not consistently documented across vitamin B12 studies^{21,22}; however, this finding could be attributed to females having a higher incidence of pernicious anemia when compared with males.^{1,4} Further evaluation is needed to study this relationship. In addition, other confounding factors such as race, diet, and culture were not independently assessed in this study and may be worth investigating in future studies.

This study aimed to further expand current knowledge of B12 deficiency in the areas of epidemiology, risk factors such as age and gender, and diagnostic issues and awareness. Hopefully, clinicians continue to effectively recognize and treat this curable disorder despite the current lack of standard diagnostic guidelines.¹⁷ Recognizing and treating vitamin B12 deficiency can have a positive impact, because therapy is simple, cost effective, and removes potential symptom overlap with other disorders, thereby improving overall patient care and quality of life.¹⁻⁴

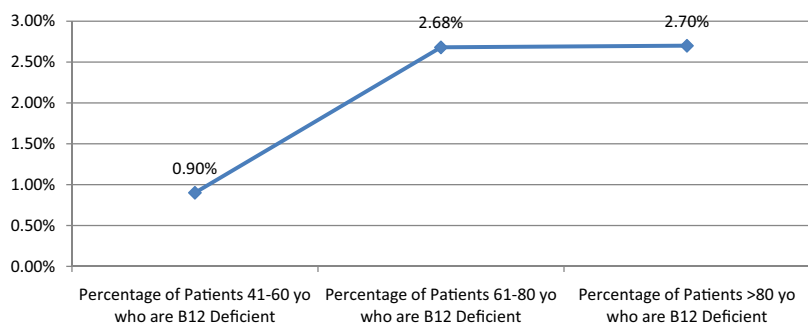


Figure 6 Office 3: Percentage of B12-deficient patients per age group relative to amount of patients per age group. Data were calculated by dividing the total number of B12-deficient patients in each age group by the total number of patients of the same age group.

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