

Vitamin B12 concentrations and clinical spectrum of apparently healthy elderly population

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ABSTRACT

Introduction : Prevalence of vitamin B12 deficiency is believed to increase with aging. The wide and non-specific spectrum of clinical presentations in patients poses a tough challenge to physicians suspecting vitamin B12 deficiency.

Objectives : This study was conducted to collect data on prevalence and clinical features of vitamin B12 deficiency in apparently healthy elderly population visiting hospitals, as the results could help rationalize and direct the appropriate management of vitamin B12 status in elderly.

Methods : This was a time bound cross sectional study where apparently healthy individuals >50 years of age were interviewed, examined and investigated in order to study their vitamin B12 concentrations and associated clinical profile.

Results: A total of 103 participants were included. The mean vitamin B12 level of the study population was 327.07 pg/ml (S.D= 268.00). In the study, 43.7% (n=45 patients) had low vitamin B12 levels (vitamin B12 deficiency) and 17.5 % (n=18 patients) had subnormal vitamin B12 levels. Among all the symptoms recorded neurological followed by cardiovascular symptoms were more commonly recorded in the patients with vitamin B12 deficiency. Distal dysesthesia was more commonly present in patients with deficient (p 0.044) than in patients with normal vitamin B12 levels. Ataxia and Romberg's sign positivity were more common in patients with vitamin B12 deficiency when compares to normal vitamin B12 levels (p 0.002 and 0.006, respectively).

Conclusion: The study shows that vitamin B12 deficiency is a common problem among elderly and the treating physician should have high index of suspicion when they present with neurological complaints.

Keywords: Cobalamin deficiency, Neurological complaints, Subnormal vitamin B12 levels, Vitamin B12 deficiency

MAIN TEXT

Introduction

Vitamin B12 (Cobalamin) deficiency is common in elderly and various studies have suggested prevalence between 3 to 40%.^(1,2,3)

Pernicious anemia though being a classical cause of vitamin B12 deficiency occurs only in a small subset of the elderly population.⁽⁴⁾

Food-cobalamin malabsorption, an inability to release cobalamin from food, is attributed mainly to atrophic gastritis and accompanying hypochlorhydria the prevalence of which increases with aging.^(5,6) However, studies reporting contradictory relationship between food-cobalamin malabsorption and aging exist and the actual relationship is yet to be established.⁽⁷⁾

As vitamin B12 is naturally found in animal products and vegetarianism is practiced more in India, the impact of insufficient intake (if any) of vitamin B12 in India is to be determined.^(8,9)

The neuropsychiatric and hematological complications are potentially serious and necessitate investigations whenever a deficiency is suspected. However, the wide and non-specific spectrum of clinical presentations in patients poses a tough challenge to physicians suspecting vitamin B12 deficiency.⁽¹⁰⁾

Also, the need for an optimal management of mild deficiency or subnormal status of vitamin B12 levels is yet to be ascertained.⁽¹¹⁾

Methods

This was a time bound cross sectional study where apparently healthy individuals >50 years of age visiting B J Medical College, Ahmedabad were interviewed, examined and investigated in order to study their vitamin B12 concentrations and associated clinical profile.

Eligibility criteria

Individuals of >50 years of age randomly selected to represent apparently healthy elderly population.

Exclusion criteria

- Individuals <50 years of age
- Individuals with history of receiving vitamin b12 supplementation in the past one year
- Individuals who have undergone surgeries like total/partial gastrectomy and gastric bypass
- Individuals who have received radiotherapy
- Critically ill
- Diagnosed cases of
 - ☞ Pernicious anemia
 - ☞ Malabsorption syndromes
 - ☞ Chronic pancreatitis
 - ☞ Immunocompromised state
 - ☞ Hypothyroidism
 - ☞ Chronic liver diseases

History and clinical examinations

Information on symptoms was obtained by structured interview. A record of anemia symptoms, cardiovascular symptoms, respiratory symptoms, genito-urinary symptoms, gastrointestinal symptoms, and neurological symptoms were made.

A history of present and previous disease was obtained. In addition, current drug use, diet patterns, and addictions were also recorded.

All patients were then subjected to thorough general examination to look for clinical signs of cobalamin deficiency. The neurological examination comprised testing for higher mental function, vibration sense, joint position sense, cutaneous sensation, postural instability, hyporeflexia, muscular strength or presence of cerebellar signs.

Investigations performed:

- a) Complete blood count
- b) Serum vitamin B12 level

Operational definition:

B12 levels were then defined as low (or deficient) if =187 pg/ml, intermediate (or subnormal) if 188-299 pg/ml and normal if =300 pg/ml.

Statistical method:

The data were analyzed using IBM SPSS Statistics v23. Continuous variables were expressed as mean \pm standard deviation (SD). Different groups were compared using non-parametric test like 2 groups Mann-Whitney U test. To compare more than two groups Kruskal-wallis H test was used and if any significant difference was seen post-hoc analysis was done to study pairwise comparison. Jonckheere-Terpstra test was used for ordinal dependent variable and for other categorical data, Pearson's Chi-square test was used. P value of <0.05 was considered significant.

Results

A total of 103 participants were included and comprised of 46 females and 57 males.

Mean age of the study population was 61.13 years (S.D=9.63). Mean age of males and females in study population were 61.28 years (S.D=10.00) and 60.94 years (S.D= 9.26) respectively.

The mean vitamin B12 level of the study population was 327.07 pg/ml (S.D= 268.00). The mean vitamin B12 levels of females and males were 351.87 pg/ml (S.D=239.43) and 307.05 pg/ml (S.D=289.56) respectively. The distribution of serum vitamin B12 levels were same between various age groups defined in the study (p 0.970) as well as between males and females (p 0.103).

In the study, 43.7% (n=45 patients) had low vitamin B12 levels (vitamin B12 deficiency) and 17.5% (n=18 patients) had subnormal vitamin B12 levels. A cumulative 61.2% (n=63 patients) had either deficient or subnormal vitamin B12 levels.

No significant difference in prevalence of deficient or subnormal vitamin B12 levels were observed between various age groups (p 0.705) or between genders (p 0.258).

Among all the symptoms recorded neurological symptoms were more commonly recorded in the patients with vitamin B12 deficiency (p 0.005) or subnormal vitamin B12 levels (p 0.048) than in patients with normal vitamin B12 levels. In the study population, 67 patients reported some or the other neurological complaints. In them 55.2% (n=35 patients) had vitamin B 12 deficiency and 20.9% (n=14 patients) had subnormal vitamin B12 levels. The rest 26.9% (n= 18 patients) had normal vitamin B12 levels.

Distal dysesthesia was the most common symptom recorded in 48.9% of vitamin B12 deficient (n=22 patients) followed by generalized weakness in 31.1% of vitamin B12 deficient (14 patients). Distal dysesthesia was also the most common complaint in patients with vitamin B12 deficiency (p 0.044) or subnormal vitamin B12 levels (p 0.001) than in patients with normal vitamin B12 levels. Generalized weakness was more common in patients with vitamin B12 deficiency (p 0.008) than in patients with normal vitamin B12 levels.

Cardiovascular symptoms were common in patients with vitamin B12 deficiency (p 0.003) than in patients with normal vitamin B12 levels. Gastrointestinal and other systemic complaints recorded when compared were not different between vitamin B12 deficient, subnormal or normal vitamin B12 level groups.

There was no significant difference in prevalence of hypertension, diabetes mellitus, chronic gastritis, coronary arterial events or cerebrovascular events between vitamin B12 deficient, subnormal or normal vitamin B12 level groups.

Mean serum vitamin B12 level in vegetarians was 291.20 pg/ml (S.D=224.42) and in non-vegetarians it was 369.81 pg/ml (S.D=308.35). However, no significant difference in prevalence of deficient or subnormal vitamin levels was found between vegetarians and non-vegetarians (p 0.394).

People who admitted having addicting habits like drinking, betel nut chewing, smoking or other forms of tobacco use were not found to have increased prevalence of vitamin B12 deficiency or subnormal vitamin B12 status (p 0.088).

Pallor, hyperpigmented knuckles, or glossitis usually described as manifestations of vitamin B 12 deficiency were also found in patients with subnormal or normal vitamin B12 levels (p values of 0.790, 0.525, and 0.804 respectively).

Prevalence of decreased muscle strength (power), ataxia, impaired joint position sense, and Romberg’s sign positivity were not same in patients with low, intermediate or normal vitamin B12 levels (p 0.009, 0.000, 0.038, 0.002 respectively). When compared pairwise, decreased muscle power and impaired joint position sense were more common in patients with vitamin B12 deficiency than in patients with normal vitamin B12 levels (p 0.017 for muscle power and 0.035 for joint position sense). Ataxia and Romberg’s sign positivity were more common in patients with vitamin B12 deficiency than in patients with subnormal (p 0.002 for ataxia and 0.015 for Romberg’s sign) or normal vitamin B12 levels (p 0.002 for ataxia and 0.006 for Romberg’s sign).

No significant difference in presence of findings like paresthesia (p 0.127), postural instability (p 0.220), impaired vibration sense (p 0.153), hyporeflexia (p 0.491), Babinski’s

sign (p 0.758), or cerebellar signs (p 0.368) were found between deficient, subnormal or normal vitamin B12 level groups.

52.4 % (n=54 patients; 30 males, 24 females) of the study population were anemic (hemoglobin =11.9 g/dl). Mean hemoglobin of the study population was 11.68 g/dl (SD 2.75). Mean hemoglobin in men was 12.00 g/dl (SD 3.07) and in women it was 11.29 g/dl (SD 2.27).

Out of 30 males with anemia, 15 (50%) had vitamin B12 deficiency, 1 (3.33%) had subnormal vitamin B12 level and 14 (46.67%) had normal vitamin B12 levels. Out of 24 females with anemia, 6 (25%) had vitamin B12 deficiency, 6 (25%) had subnormal vitamin B12 levels and 12 had normal vitamin B12 levels.

Mean hemoglobin of participants in vitamin B12 deficient group was 12.24 g/dl (S.D=2.49). In participants with subnormal and normal vitamin B12 levels the mean hemoglobin was 12.33 g/dl (S.D=3.05) and 10.76 g/dl (S.D=2.70), respectively. The distribution of hemoglobin across various age groups defined in the study as well as their distribution between males and females were same (p values of 0.290 and 0.064 respectively). Also there was no difference in prevalence of anemia across various age groups (p 0.294) or between genders (p 0.963). However, the mean hemoglobin levels and the prevalence of anemia were significantly different between participants with low and normal vitamin B12 levels (p 0.029 and 0.040, respectively).

Tables and figures: To be placed along with results.

Table 1: Mean vitamin B12 levels across various age groups

Age group (in years)	Mean Vitamin B12 (pg/ml)	Std. Error
50-59	321.063	36.3201
60-69	354.452	59.0369
70-79	285.722	40.6070
80-89	350.800	164.5471

Table 2: Age-group wise and gender wise distribution of vitamin B12 levels

Age (years)	Gender					
	Females (n=46)			Males (n=57)		
	Low	Intermediate	Normal	Low	Intermediate	Normal
50-59	9	4	10	12	6	7
60-69	3	2	7	11	2	6
70-79	2	3	3	5	1	4

80-89	2	0	1	1	0	1
90-99	0	0	0	0	0	1
Total (n=103)	n=16	n=9	n=21	n=29	n=9	n=19

Figure 1: Vitamin B12 status in study population

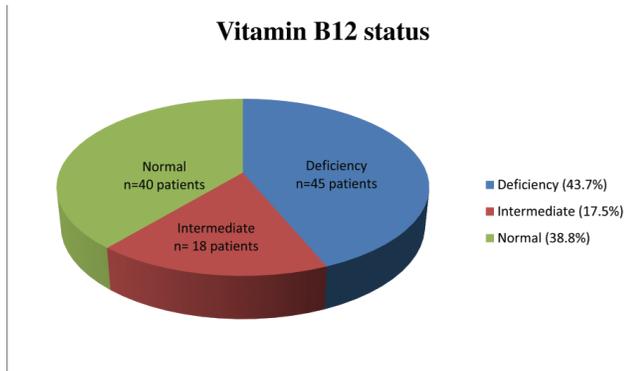
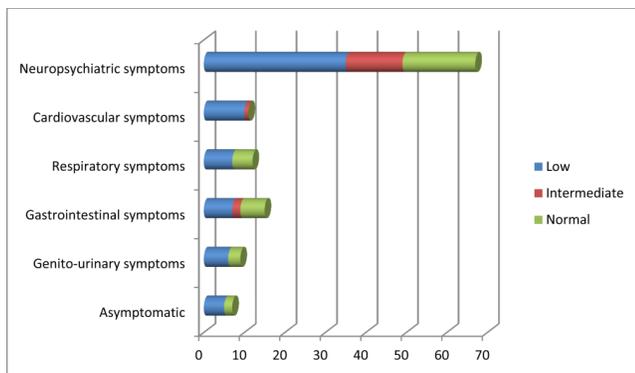


Figure 2: Clinical profile of patients with low, intermediate and normal vitamin B12 levels



Note: Numbers along X-axis indicates the number of participants in whom the complaints were recorded.

Figure 3: Clinical profile of patients with vitamin B12 deficiency (n= 45)

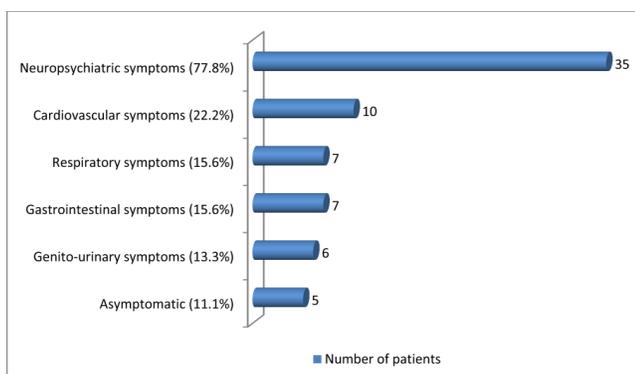


Figure 4: Distribution of hemoglobin between females and males

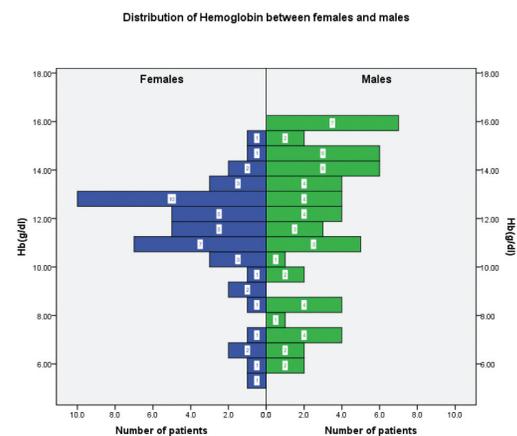
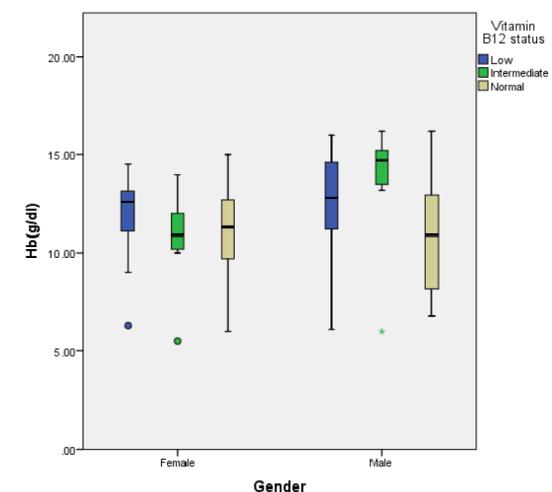


Figure 5: Distribution of hemoglobin across vitamin B12 status in females and males



Discussion

The present study which included 103 participants with 57 males and 46 females showed that the prevalence of vitamin B12 deficiency was 43.7% (45 patients) in elderly aged above 50 years. These results were similar to study by Refsum et al which reported vitamin B12 deficiency in 47% of population aged between 27 and 55 years. On further tests 73% of the study population in Refsum et al would show metabolic signs of vitamin B12 deficiency.⁽¹²⁾ In the present study, 63 patients (61.2%) had vitamin B12 levels considered deficient or subnormal.

Fernandes-Costa et al (1985) had previously reported significantly higher serum B 12 values in females than in males with mean serum B 12 values of 819 and 647pg/mL in females and males.⁽¹³⁾ Other investigators have reported similar findings.^(14,15) However studies that have found no difference in mean B 12 values between both sexes also exist.⁽¹⁶⁾ In the present study too the mean vitamin B12 levels were greater in females than in males with the mean vitamin B12 level of females and males being 351.87 pg/ml (S.D=239.43) and 307.05 pg/ml (S.D=289.56) respectively and was not significantly different. Taken together, the study does not provide sufficient evidence on which to predict a difference in B 12 status by gender.

Though some studies in the past have reported age related decline in vitamin B12 levels owing to increasing prevalence of atrophic gastritis in elderly contradictory studies also do exist.^(16,17,18,19) In the present study, vitamin B12 doesn't seem to significantly decrease with aging suggesting that aging alone may not be the risk factor for developing vitamin B12 deficiency.

Neurological system was the most commonly involved system with distal dysesthesia followed by generalized weakness being the most common complaints. Neurological complaints were documented in 77.8% of patients with vitamin B12 deficiency (35 out of 45) and the same percentage of people with subnormal vitamin B12 levels (14 out of 18) which was similar to the results observed by Heaton et al (1991) and Savage et al (1994) who reported neurological complications in 75-90% of their study population.^(20,21) 29.55% (n=13 out of 44) of the patients with distal dysesthesia and 20% (n=4 out of 20) of the patients with generalized weakness in the study population had subnormal vitamin B12 levels and not frank deficiency implying that treatment should be considered even in patients with subnormal vitamin B12 levels.

Though cardiovascular symptoms like chest discomfort and palpitations were reported more often in patients with vitamin B12 deficiency, majority of those who reported these complaints also had anemia which could have interfered with the results.

Studies have shown B12 deficiency as an independent risk factor for cerebrovascular and coronary events.^(22,23) However, in the present study, such association of vitamin B12 deficiency was not seen with coronary artery events or cerebrovascular events. This discrepancy could be attributed to small study sample.

In the study both vegetarians and non-vegetarians were equally prone to develop vitamin B12 deficiency which contradicts other studies which reported increased deficiency in vegetarians.^(24,25,26) This finding possibly indicates that non-vegetarians in India are only "occasional" meat eaters.

Smoking, alcohol and tobacco use are known risk factors for deficiency of many vitamins including vitamin B12.^(8,27,28) In the present study, people who admitted having addicting habits were not found to have increased prevalence of vitamin B12 deficiency or subnormal vitamin B12 status. However, strong inferences were not made as the details regarding the type or severity of addicting habits were not collected. It will be interesting to see if any association between various addicting habits and vitamin B12 deficiency will be found in future studies.

Pallor, hyperpigmented knuckles, or glossitis are usually described as manifestations of vitamin B 12 deficiency.⁽²⁹⁾ These features were also present in non-deficient population and cannot be considered as reliable indicators.

Neurological manifestations of vitamin B12 deficiency include sensory disturbances in the extremities, impairment of vibratory and position sense, motor disturbances, cognitive changes, visual disturbances, insomnia, impotency, and impaired bowel and bladder control.^(8,30,31) In the study, neurological findings like paresthesia, postural instability, impaired vibration sense, hyporeflexia, Babinski's sign, or cerebellar signs were also found in population with subnormal or normal vitamin B12 levels. Therefore these cannot be considered as credible indicators of vitamin B12 deficiency, at least in elderly.

Decreased muscle power and impaired joint position sense were more common in patients with vitamin B12 deficiency when compared with the normal participants. However their prevalence was same when it was compared with participants with subnormal vitamin B12 levels (p 1.00 for decreased power, p 1.000 for impaired joint position sense). Therefore their presence may indicate deficient or subnormal vitamin B12 status.

Ataxia and Romberg's sign positivity were seen commonly in patients with vitamin B12 deficiency than in patients with subnormal or normal vitamin B12 levels and could be more specific indicators of vitamin B12 deficiency.

Thus the present study suggests that most of the patients could be developing neurological manifestation much before they develop overt vitamin B12 deficiency, once again, reinforcing the thought of considering treatment of patients with subnormal vitamin B12 levels, though not agreed by everyone.⁽¹¹⁾

In the present study, which consisted of participants above 50 years of age, aging or gender did not influence the distribution of hemoglobin or prevalence of anemia (hemoglobin =11.9 g/dl). Surprisingly when hemoglobin distribution was studied against vitamin B12 levels of the population it was found that the population with normal vitamin B12 levels had lower mean hemoglobin levels when compared to patients with deficient or subnormal vitamin B12

status, indicating that there were other causes of anemia which have to be considered while evaluating anemia in the elderly population with anemia of chronic disease and iron deficiency probably still being the common culprits.^(32,33)

Conclusion

The present study shows that vitamin B12 deficiency is a common problem among elderly and the treating physician should have high index of suspicion when elderly patients present with neurological complaints like distal dysesthesia and weakness. Detailed neurological examination should be performed even in asymptomatic elderly patients and if findings consistent with vitamin B12 deficiency are found treatment should be considered, even when vitamin B12 levels are found to be subnormal. Anemia, glossitis etc. are classical but not the common features of vitamin B12 deficiency and cannot be considered as reliable indicators of vitamin B12 deficiency. Future prospective and interventional studies with larger population and vitamin B12 supplementation will help in proposing stronger recommendations with respect to treatment of patients with subnormal vitamin B12 levels.

Limitations

- This study conducted in apparently healthy population visiting health care need not be necessarily healthy and may not be representative of general elderly population.
- Small study population
- Absence of structured tool to assess dietary intake of vitamin B12 or details regarding addicting habits.

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