

Vitamin B12 deficiency in a large cohort of healthcare professionals across the network of an eyecare organization in India

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Purpose: To evaluate Vitamin B12 levels in healthcare professionals at a tertiary eyecare centre in India. **Methods:** This was a cross-sectional study conducted among healthcare professionals working at a tertiary eyecare centre in India. The sample included 2,374 employees. Chemiluminescent immunoassay method (reference range, 211–911 pg/ml) was used to assess serum vitamin B12 levels. Effect of age and gender was analyzed in vitamin B12 normal and vitamin B12 deficient groups. To evaluate risk factors, questions related to vitamin B12 deficiency were asked to the study participants in a survey. **Results:** The mean age of employees was 29.2 ± 0.7 years. Around 26% of them were vitamin B12 deficient. The proportion of males in the vitamin B12 deficient group (61.2%) was significantly higher ($P < 0.0001$) than that of the vitamin B12 normal group (44.9%). There was no effect of age on vitamin B12 levels in both vitamin B12 normal and vitamin B12 deficient groups. Mean vitamin B12 levels in males (289.1 ± 22.2 pg/ml) was significantly lower ($P < 0.0001$) than that of females (338.7 ± 30.0 pg/ml). **Conclusion:** This is the first such study on eyecare professionals. One-fourth of the eyecare professionals were vitamin B12 deficient. The proportion of males was higher in the vitamin B12 deficiency group. Males had lower vitamin B12 levels than females. Annual blood tests for vitamin B12 are recommended for timely diagnosis and management of vitamin B12 deficiency, particularly in males.

Key words: Age factors, gender, health professional, occupational health, vitamin B12 deficiency

Vitamins are the most essential micronutrients that help in the proper functioning of the body's metabolism. Vitamin B12, also known as cyanocobalamin, is a water-soluble vitamin. It is mostly found in animal foods such as meat, milk products, and poultry. It helps in normal functioning of the nervous system, red blood cell formation, supporting bone health, avoiding birth defects, supporting healthy skin and hair, and avoiding depression. The normal range of serum vitamin B12 level is 200–900 pg/ml. According to the Food Safety and Standards Authority of India (FSSAI), the recommended dietary allowance is 1 µg/day.

Vitamin B12 deficiency is manifested mostly when there are increased requirements such as adolescence and pregnancy. Prevalence of deficiency is not associated with the level of development as measured by human development index or geographical location, and is much more in vegetarians than non-vegetarians.^[1,2] It is also significantly reduced in individuals using metformin.^[3] Fortification of food with B12 helps in reducing the deficiency of B12. Hence, the meals in schools were fortified and the exercise showed good results in the past.^[4] Vitamin B12 deficiencies can cause anemia, autonomic

neuropathy, cancers, cardiovascular diseases, cerebrovascular diseases, generalized weakness, loss of appetite, mental health issues, myalgia, and neural tube defects.^[5] Most common causes of deficiency are due to either severe malabsorption by autoimmune gastritis, bowel diseases or gastrectomy, or by use of drugs that can cause malabsorption, and less dietary intake.^[6]

Several studies were done in the past to evaluate vitamin B12 levels in a wide range of populations like infants, pre-school children, school-aged children, pregnant and lactating women, women of reproductive age, adults, elderly, metformin treated individuals, vegetarians, lacto vegetarians, lacto-ovo vegetarians, non-vegetarians, active women (athletes), and sedentary women.^[1,7,8] However, there is a paucity of literature on B12 deficiency in the eyecare workforce.^[9] Therefore, the purpose of this study was to evaluate vitamin B12 levels in a large pool of healthcare professionals working at a tertiary eyecare centre in India.

Methods

It was a cross-sectional study approved by the Institutional Ethics Committee and was carried out in accordance with

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The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The study plan and procedures were explained to the participants and informed consent was obtained from the study subjects.

All employees working at a tertiary eye care centre in India across multiple centers in the states of Andhra Pradesh, Karnataka, Odisha, and Telangana were included in the study. Categories of employees included administrators, nurses, ophthalmologists, opticians, optometrists, public health workers, scientists, lab technicians, students, vision technicians, etc., Blood samples were collected between July and August 2019 by following standardized procedures for the collection of blood samples. There was no intake of vitamin B12 supplements by any employee at the time of blood collection. Samples were analyzed for serum vitamin B12 levels by chemiluminescent immunoassay method (reference range, 211–911 pg/ml). Serum vitamin B12 values less than 211 pg/ml were considered vitamin B12 deficient.

To evaluate risk factors of vitamin B12 deficiency, questions were asked to the study participants in a survey using Google Forms (Google LLC, Mountain View, CA, USA). The survey questions to the study subjects included dietary preferences, family history of vitamin B12 deficiency, history of stomach or intestine diseases or infections, history of immune disorders or chronic pancreatitis, history of stomach or intestinal surgery, history of diabetes mellitus, intake of medications such as colchicine, chloramphenicol, ethanol, histamine 2 receptor antagonists, metformin, and proton pump inhibitors, and status on pregnancy and lactation.

The statistical analysis was performed using STATA version 14.2 (StataCorp, College Station, TX, USA). Descriptive statistics included mean \pm standard error and proportions. Data were categorized into vitamin B12 deficient and vitamin B12 normal groups. Age, gender, and risk factors from survey were compared between two groups by mixed effects model with random intercepts at levels of eye care and state. Factors associated with vitamin B12 deficiency was evaluated by multilevel mixed effects regression. A *P* value of <0.05 was considered statistically significant.

Results

A total of 2,374 employees were evaluated. Mean age of employees was 29.2 ± 0.7 years. Males numbered 1,164 (49%), while 1,210 (51%) were females. Mean vitamin B12 level was 314.0 ± 28.8 pg/ml. A total of 606 employees (25.5%) had vitamin B12 below normal range [Table 1]. Mean age in vitamin B12 normal group (30.6 ± 0.4 years) was comparable ($P = 0.60$) to the mean age in vitamin B12 deficient group (29.2 ± 0.7 years). The proportion of males was significantly higher ($P < 0.0001$) in vitamin B12 deficient group ($n = 371$, 61.2%) than vitamin B12 normal group ($n = 793$, 44.9%).

Table 2 shows the results of survey responses that were provided on a voluntary basis by a total of 208 respondents. Nearly 20% were strict vegans, 51% were either predominantly or strict vegans, 14% had a positive family history of vitamin B12 deficiency, 6% had a history of stomach or intestine diseases or infections, 7% has a history of immune disorders or chronic pancreatitis, none had a history of stomach or intestinal surgery, 3% had diabetes mellitus, 5% had an intake of medications

Table 1: Vitamin B12 in eyecare professionals. This table summarizes age, gender, and vitamin B12 in employees of a tertiary eyecare center with vitamin B12 deficient and vitamin B12 normal levels

Parameter	Vitamin B12 deficient	Vitamin B12 normal
Age (years), mean \pm SE	30.6 \pm 0.4	29.2 \pm 0.7
Male:Female (% males)	371:235 (61.2%)	793:975 (44.9%)
Vitamin B12 in all (pg/ml)		
<i>N</i> (%)	606 (25.5%)	1768 (74.5%)
Mean \pm SE	182.2 \pm 2.3	340.8 \pm 18.9
Minimum	99	211.1
Maximum	210	2000
Vitamin B12 in males (pg/ml)		
<i>N</i> (%)	371 (31.9%)	793 (68.1%)
Mean \pm SE	181.1 \pm 2.4	316.7 \pm 17.7
Minimum	99	211.1
Maximum	210	2000
Vitamin B12 in females (pg/ml)		
<i>N</i> (%)	235 (19.4%)	975 (80.6%)
Mean \pm SE	183.9 \pm 2.5	363.3 \pm 17.6
Minimum	119	211.1
Maximum	210	2000

(SE: standard error)

that can cause vitamin B12 deficiency, and 2% were either pregnant or lactating. None of these factors were significantly different between the Vitamin B12 deficient and Vitamin B12 normal groups. There was no significant difference ($P = 0.47$) in the vitamin B12 levels between survey responders (306.5 ± 30.4 pg/ml) and non-responders (314.5 ± 28.6 pg/ml).

Table 3 shows the results of analysis of risk factors for vitamin B12 deficiency by regression analysis. Multilevel mixed effects model showed only male gender to be a significant ($P < 0.0001$) risk factor associated with vitamin B12 deficiency in our cohort. Mixed effects logistic regression analysis found the odds ratio for male gender to be 1.94 ± 0.19 (95% confidence interval, 1.61 to 2.34). Mean vitamin B12 levels in males and females were 289.1 ± 22.2 pg/ml and 338.7 ± 30.0 pg/ml respectively, the difference between the two being statistically significant ($P < 0.0001$).

Discussion

The identification and treatment of vitamin deficiencies are very important as the consequences of deficiencies are very severe in the long term. Vitamin B12 supplements can reverse conditions like glossitis, megaloblastic features in bone marrow, cardiomyopathy, delusions, paresthesia, ataxia, psychosis, etc.^[10] Vitamin B12 deficiency causes anemia, giddiness (fainting episodes), lethargy, myalgia, muscle cramps, palpitations, shortness of breath and syncopal attacks, and all of these can impact the efficiency of young working people. Vitamin B12 deficiency is a masquerade which needs much more attention with early diagnosis and appropriate treatment. There were several attempts in the past to evaluate Vitamin B12 deficiency in India.

Singla *et al.*^[11] conducted a retrospective, cross-sectional study and showed that 47% of the population were Vitamin B12 deficient (<200 pg/ml). In a study conducted in urban and

Table 2: Risk factor analysis of vitamin B12 in eyecare professionals. This table summarizes the responses to survey by employees of a tertiary eye care centre

Question related to B12 deficiency	All employees (208 respondents)	Vitamin B12 deficient (n=81)	Vitamin B12 normal (n=127)	P
Strict vegan	41 (19.7%)	18 (22.2%)	23 (18.1%)	0.43
Predominantly or strictly vegan	107 (51.4%)	41 (50.6%)	66 (52.0%)	0.85
Family history*	15/110 (13.6%)	8/45 (17.8%)	7/65 (10.8%)	0.29
Stomach or intestine diseases or infections	12 (5.8%)	5 (6.2%)	7 (5.5%)	0.53
Immune disorders, human immunodeficiency virus infection or chronic pancreatitis	15 (7.2%)	4 (4.9%)	11 (8.7%)	0.31
Diabetes mellitus	6 (2.9%)	1 (1.2%)	5 (3.9%)	0.26
Pregnancy and lactation**	2/92 (2.2%)	1/35 (2.9%)	1/57 (1.8%)	0.73
Intake of medications	10 (4.8%)	3 (3.7%)	7 (5.5%)	0.55

(*Available only from 110 respondents; **Applicable only on 92 respondents)

Table 3: Regression analysis for vitamin B12 deficiency. This table summarizes the results of analysis of risk factors for vitamin B12 deficiency by multilevel mixed effects regression analysis

Risk factor	P	Co-efficient±standard error	95% confidence intervals
Age	0.56	-0.0005±0.0009	-0.0023 to 0.0013
Male gender	<0.0001	0.10±0.02	0.07 to 0.13
Strict vegan	0.42	0.07±0.08	-0.10 to 0.23
Predominantly or strictly vegan	0.89	-0.10±0.07	-0.14 to 0.12
Family history	0.26	0.15±0.13	-0.11 to 0.41
Stomach or intestine diseases or infections	0.49	0.10±0.14	-0.18 to 0.38
Immune disorders, human immunodeficiency virus infection or chronic pancreatitis	0.25	-0.15±0.13	-0.40 to 0.10
Diabetes mellitus	0.26	-0.22±0.20	-0.61 to 0.17
Pregnancy and lactation	0.73	0.12±0.35	-0.56 to 0.80
Intake of medications	0.41	-0.13±0.16	-0.43 to 0.18

rural middle-aged men, it was found that 67% were vitamin B12 deficient.^[12] The main causes for the deficiency are found to be insufficient dietary intake and residing in a geographical region with a maximum population following a vegetarian diet.^[13] However, our study is mainly focused on specific population, that is, healthcare professionals. Healthcare workers are considered as connecting links between medical science and community health. Hence, the good health of medical professionals is very important for maintaining the health of the community. In the current study, we report vitamin B12 levels in healthcare professionals working at a tertiary eyecare centre, and found that one-fourth of the eyecare professionals were deficient in vitamin B12.

A cross-sectional study conducted among company executives in India revealed that 65% were deficient (<193 pg/ml). This study also included a second phase where supplementations and recommendations required to improve vitamin B12 levels were given and that showed positive results. However, this study was done in a limited sample of 75 executives, and concluded that vegetarian diet consumption and insufficient consumption of dairy products, poultry, and meat were the main reasons for B12 deficiency. All participants were males and hence, the effect of gender could not be assessed.^[14] In contrast, we found only 25% of eyecare workforce to be vitamin B12 deficiency.^[11,12,14] This may be due to several reasons. Firstly, due to changes in food

habits and taste preferences: In recent years, meat consumption has increased with the improvement in economic growth in developing countries.^[15] Secondly, due to the precautionary measures of healthcare professionals, nutritional awareness is better among them than the general population.

A population-based study in Jordan showed that there is no effect of gender on vitamin B12 deficiency.^[16] In our study, the proportion of males was significantly higher in vitamin B12 deficient group (~61%) than the vitamin B12 normal group (~45%). In a cross-sectional study with a large cohort (n = 7963), around 23% were identified with vitamin B12 deficiency. The authors also found that number of males in vitamin B12 deficiency group (74.8%) was significantly higher (P < 0.0001) than in vitamin B12 normal group (67%), trend being similar to our study. The authors speculated that dietary levels or hormonal levels did not explain conclusions such as men had a significantly higher prevalence of vitamin B12 deficiency. Genetic polymorphism within the local population can be a reason for an association of gender with vitamin B12 levels.^[17] In our study, mean vitamin B12 level was significantly higher in females (339 pg/ml) than males (289 pg/ml). The frequency of hyperhomocysteinemia is significantly higher in males.^[18] This may explain lower vitamin B12 in males and future studies may evaluate the levels of homocysteine also.

The effect of age on vitamin B12 levels is controversial. Green *et al.*^[19] reviewed several studies and concluded that

during infancy and adolescence, when rapid growth takes place, there is a high demand for vitamin B12 and this could lead to vitamin B12 deficiency. It is a known fact that absorption of Vitamin B12 decreases with age, and hence deficiency increases; but most of the studies which made this conclusion had mean age >70 years or more number of people in old ages.^[20-22] In our study, we did not find any effect of age on vitamin B12 levels and the median age between the vitamin B12 normal and vitamin B12 deficient groups was found to be comparable.

The strengths of this study are large sample size, and first of its kind in eyecare professionals. This is also the first study to report vitamin B12 levels in health care professionals in India. A review by Green *et al.*^[19] postulates that the deficiency of B12 might be due to eating less vitamin B12 rich foods like meat. However, in our study, food preferences did not appear to be associated with vitamin B12 deficiency. Not only food habits, but also there was no relationship between family history, presence of stomach infections, immunity disorders, diabetes mellitus, pregnancy, lactation, and intake of medications, and Vitamin B12 deficiency in our cohort. A limitation is that we included only eyecare professionals. Further, the response rate for the questionnaire among the study participants was low (<10%). Future studies can also consider intrinsic factor blocking antibody (IFBA) testing. The intrinsic factor is required for the absorption of vitamin B12 and the testing is indicated to confirm pernicious anemia. In pernicious anemia, antibodies to intrinsic factor producing gastric parietal cells are produced which cause intrinsic factor deficiency, B12 anemia and other debilities.

Conclusion

In conclusion, vitamin B12 deficiency is moderately prevalent among eyecare professionals in India. Bearing in mind the severe ill effects of long-term vitamin B12 deficiency and its subclinical features in the early stage, annual biochemical screening of employees and appropriate management via supplements are recommended. Males are at higher risk of being vitamin B12 deficient. Dietary suggestions to consume animal-based food products (such as egg and meat), milk and milk-based products, and non-animal-based ones (such as fortified cereals, mushrooms, nutritional yeast, plant-based milk, and sea weeds) to improve serum vitamin B12 levels might be beneficial.

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Conflicts of interest

There are no conflicts of interest.

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