

Original Research Article

Predictors of vitamin B12 deficiency among patients with skin hyperpigmentation attending the dermatology clinic at Acharya Vinoba Bhave rural hospital Wardha, India

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ABSTRACT

Background: India like any other developing country is grappling with malnutrition cases due to avoidable factors. Nutritional deficiencies are prevalent in India and hyperpigmentation due to micronutrient deficiencies are common. Prevalence of B12 deficiency varies from 3% to 5% in the general population. This study aimed to determine the predictors of vitamin B12 deficiency among patients with skin hyperpigmentation AVBRH hospital, India.

Methods: A cross-sectional study involving 164 patients with skin hyperpigmentation at dermatology department of AVBRH hospital, India was conducted from 1st April to June 30th 2024. Interviewer-administered questionnaires were used to obtain data and analysis was done using Stata version.

Results: Of the 164 respondents, 73(44%) had vitamin B12 deficiency. The mean plasma vitamin B12 level was 201 pg/ml among strict vegans as compared to 314 pg/ml in non-strict vegans. Young age (OR=7.1; 95%CI: 1.120-2.737; p=0.009), distance more than 5 kilometers from nearest health facility (OR=3.8, 95%CI: 0.024-0.187; p=0.005), not employed (OR=2.5, 95%CI: 0.731-4.071; p=0.026), being strict vegetarian (OR=2.1, 95%CI: 0.141-1.050; p=0.002), and number of meals less than 3 per day (OR=9.1; 95%CI: 3.14-7.320, p=0.005) were independently associated with vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH hospital, India.

Conclusions: The prevalence of Vitamin B12 deficiency among patients with skin hyperpigmentation is high in India. Young age, residing more than 5 kilometers from health facility, being a strict vegetarian, having less than 3 meals per day and unemployment are predictive for vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH hospital.

Keywords: Vitamin B12 deficiency, Skin hyperpigmentation, Predictors of deficiency, Dermatology clinic, Acharya Vinoba Bhave rural hospital, Wardha, India, Patient health correlates

INTRODUCTION

India like any other developing country is grappling with malnutrition cases due to avoidable factors. In developing countries like India, nutritional deficiencies are prevalent and hyperpigmentation due to protein energy malnutrition, zinc deficiency and pellagra are common.¹ Prevalence of B12 deficiency varies from 3% to 5% in the general population and 5% to 20% among people older than 65 years.²

Vitamin B12 deficiency is a global health concern, with significant variations in prevalence based on geographic location, dietary habits, and socioeconomic factors. In India, vitamin B12 deficiency is particularly prevalent due to the high prevalence of vegetarianism and low intake of animal products, which are primary sources of vitamin B12.³ Studies in various Indian populations have reported vitamin B12 deficiency rates ranging from 47% to 70%, depending on the population studied and the diagnostic criteria used.^{4,5}

Patients with skin hyperpigmentation, especially in rural settings like Acharya Vinoba Bhave Rural Hospital, may be at higher risk of vitamin B12 deficiency. Hyperpigmentation is a recognized clinical manifestation of vitamin B12 deficiency, typically associated with darker-skinned individuals who might not easily recognize subtle skin changes.⁶ The exact prevalence of vitamin B12 deficiency among this subgroup, however, remains underexplored, underscoring the importance of targeted research in this area.

The production of red blood cells and the proper operation of the brain and nervous system depend heavily on vitamin B12, a water-soluble vitamin. It is one among the most complicated vitamins chemically, featuring a cobalt atom at the heart of a corrin ring. Several cobalamin forms, such as methylcobalamin and 5-deoxyadenosylcobalamin, which are active in human metabolism, can be formed when the cobalt atom coordinates with different groups.⁷ Humans mostly obtain vitamin B12 from animal-derived foods such as meat, dairy products, and eggs. Some bacteria and archaea can synthesize this vitamin. Following its binding to intrinsic factor, a glycoprotein released by the parietal cells of the stomach, vitamin B12 is absorbed in the ileum.⁸

The human body uses vitamin B12 for two main metabolic processes. It first serves as a cofactor for methionine synthase, which is necessary for the conversion of homocysteine to methionine, a step that is vital for the methylation and DNA synthesis processes. Second, it acts as a cofactor for L-methylmalonyl-CoA mutase, which is essential for the metabolism of fatty and amino acids because it changes methylmalonyl-CoA into succinyl-CoA. When these processes are interfered with by a vitamin B12 shortage, homocysteine and methylmalonic acid buildup occur, which can cause

neurological, hematological, and gastrointestinal problems.⁹

Red blood cell development and maturation, neuron health, and the synthesis of myelin, the protective sheath that envelops nerve fibers, all depend on vitamin B12.¹⁰ Additionally, vitamin B12 is essential for DNA synthesis and repair, especially in cells that divide quickly, such as those in the gastrointestinal tract and bone marrow.⁷

The recommended daily allowance (RDA) for vitamin B12 is 2.4 micrograms for both men and women aged 10 to 50. This sum is thought to be adequate to cover the needs of almost everyone in this age range. The RDA is raised to 2.6 micrograms per day for pregnant women in order to support the growing fetus's neurological function and the increased demand for DNA synthesis. For nursing mothers, the RDA is raised to 2.8 micrograms per day in order to guarantee that breast milk contains enough vitamin B12 for the nursing infant.¹¹ Even though the recommended daily allowance (RDA) for vitamin B12 for people over 50 is still 2.4 micrograms, it is advised that they get their vitamin B12 from fortified foods or supplements because of the higher risk of malabsorption problems in this age group.¹²

A plasma concentration of less than 239 pg/ml is considered a vitamin B12 deficiency, whereas a value of 239–931 pg/ml is considered normal. Consuming meat, poultry, and dairy products is the primary way that humans obtain vitamin B12, also known as cobalamin. Although the majority of people in India are vegetarians, their diets only provide a small amount of vitamin B12.

The recommended dietary allowances (RDA) change with age.^{2,13} Vitamin B12 insufficiency is common among Indian women and children, particularly vegetarians. A lack of vitamin B12 might manifest as dementia, gastrointestinal problems, neurological defects, or anemia. Rarely does vitamin B12 insufficiency manifest as hyperpigmentation. In India, a retrospective analysis of 63 patients with neurological disorders linked to vitamin B12 deficiency revealed that almost one fifth of patients (19%) also have hyperpigmentation.¹⁴

METHODS

Study place

A hospital based cross-sectional study was carried out at the dermatology clinic of AVBRH Hospital located in Wardha district, India from April 1st 2024 to June 30th 2024.

Sample size

The study population was all patients with skin hyperpigmentation receiving clinical services from the dermatology clinic of AVBRH Hospital.

Inclusion criteria

Inclusion criteria included all patients aged 10-50 years with skin hyperpigmentation receiving clinical services from the dermatology clinic of AVBRH Hospital who consented to the study.

Exclusion criteria

Exclusion criteria were patients with known autoimmune disease that contribute to vitamin B12 deficiency such as pernicious anemia. A total of 164 participants were considered for this study using consecutive sampling method.

Patients with skin hyperpigmentation who met the inclusion criteria were given questionnaires and informed consent to participate in the study after receiving thorough explanations and counseling. After locating a suitable vein and cleaning the puncture site with a 70% alcohol swab, a hypodermic needle was placed inside the vein. Four to six milliliters of venous blood were drawn using a syringe and then placed in sterile, red and purple top vacutainers. This was subsequently transferred to the AVBRH hospital's laboratory for prompt examination of the complete blood count and serum vitamin B12.

Statistical analysis

The data was checked for accuracy before the subject left the interview. Excel 2016 was used to code, enter, and export data to STATA 14.2. The analysis was conducted with the objectives in mind. For the first aim, the number of patients with skin hyperpigmentation divided by the total number of patients with vitamin B12 insufficiency and then multiplied by 100 was used to calculate the prevalence of vitamin B12 deficiency among patients with skin hyperpigmentation. A pie chart with the 95% CI was used to display this as a percentage.

Using univariate analysis, the second objective was to determine the prevalence of the factors linked to vitamin B12 insufficiency in individuals with skin hyperpigmentation. In order to control for confounding, all factors with a p value less than 0.2 were taken into consideration for multivariate analysis after each variable was compared with the prevalence of vitamin B12 insufficiency using the chi square test at bivariate analysis. Logistic regression was used for multivariate analysis, and variables with a p value less than 0.05 were deemed significant.

RESULTS

Basic characteristics of study participants

We enrolled 164 participants into the study with a response rate of 100%. The majority of the participants were aged between 20 and 29 years, 80 (49%), were females 115 (70%) of rural residence, 126 (77%), single

121 (74%) and of tertiary level of education, 129 (79%). Most participants were not employed, 139 (85%) and lived in a distance of 5 kilometers and more from a health center, 97 (59%). Majority of our respondents were Hinduism by religion 122 (74%). Majority were strict vegetarian; that is 83 (51%) and had more than 3 meals per day 106 (64.6%) with no gastrointestinal disorder 146 (89%). Most of our respondents had normal levels of hemoglobin 95 (57.9%) and plasma vitamin B12 levels 92 (56%).

Prevalence of vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH hospital, India

Out of the 164 respondents who were diagnosed with skin hyperpigmentation and considered for the study, 73(44%) had vitamin B12 deficiency. This is illustrated in Figure 1.

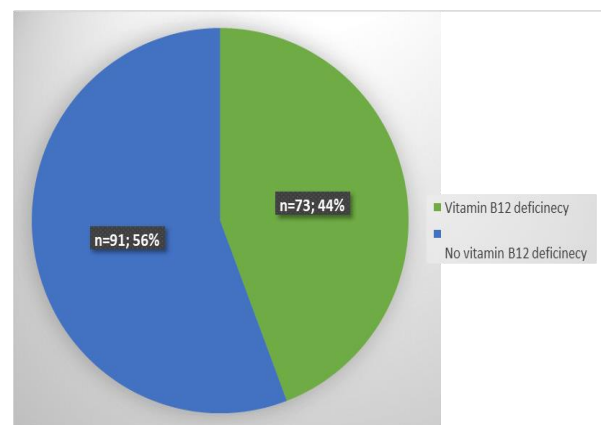


Figure 1: Prevalence of vitamin B12 deficiency among patients with skin hyperpigmentation.

Mean plasma vitamin B12 levels

The mean plasma vitamin B12 level among strict vegetarian participants was 201 unit at 95% confidence interval of 201 ± 10.2 . This is presented in Table 1.

Associated factors of vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH

Bivariate analysis shows several significant variables such as age, marital status, distance from nearby health center, employment status, presence of GIT disorder, strict vegetarian, number of meals per day and hemoglobin levels.

Multivariable analysis revealed that age category of 20-29 years (OR=7.1; 95%CI: 1.120-2.737; $p=0.009$), distance more than 5 kilometers from nearest health facility (OR=3.8, 95%CI: 0.024-0.187; $p=0.005$), not employed (OR=2.5, 95%CI: 0.731-4.071; $p=0.026$), being strict vegetarian ((OR=2.1, 95%CI: 0.141- 1.050; $p=0.002$), and reduced number of meals less than 3 per

day (OR=9.1; 95%CI: 3.14-7.320, p=0.005) were independently associated with vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH. It was also observed that patients who had less than 3

meals per day were 9.1-fold the odds of having low vitamin B12 and skin hyperpigmentation. Likewise, patients who were strict vegetarians were 2.1-fold of having vitamin B12 deficiency.

Table 1: Mean plasma vitamin B12 among strict vegetarian and non-strict vegetarian.

Strict vegetarian	Frequency	Mean plasm vitamin B12(pg/dl)	Standard deviation (SD)	95% CI
Yes	81	201	50.4	201±10.2
No	83	314	91.6	314±16.5

CI = Confidence interval

Table 2: Bivariate analysis of associated factors of vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH (n=164).

Variable	Category	Plasma vitamin B12 Levels		cOR(95%CI)	P value
		Low (n=73)	Normal (n=91)		
Socio-demographic factors					
Age in years	10-19	18 (32.7)	37 (67.3)	2.3(0.789-6.606)	0.128*
	20-29	42 (52.5)	38 (47.5)	1.1(0.369-2.737)	0.992
	30-39	10 (52.6)	9 (47.4)	2.6(0.510-13.16)	0.118*
	40-50	3 (30)	7 (70)	1.00	
Residence	Rural	56 (44.4)	70 (55.6)	1.2(0.487-2.099)	0.975
	Urban	17 (44.7)	21 (55.3)	1.00	
Gender	Female	51 (44.3)	64 (55.7)	1:00	
	Male	22 (44.9)	27 (55.1)	1.0(0.499-1.915)	0.948
Marital status	Single	49 (40.5)	72 (59.5)	2.3(1.069-4.745)	0.033*
	Married	1 (20)	4 (80)	6.1(0.623-60.31)	0.120*
	Widow	23 (60.5)	15 (39.5)	1.00	
Level of education	Primary	6 (60)	4 (40)	0.5(0.137-1.899)	0.317
	Secondary	11 (44)	14 (56)	0.9(0.411-2.314)	0.957
	Tertiary	56 (43.4)	73 (56.6)	1.00	
Distance from NHC	≤ 5km	20 (24.4)	62 (75.6)	1.00	
	> 5km	53 (64.6)	29 (35.4)	4.4 (0.089-0.347)	<0.001*
Employment status	Employed	14 (56)	11 (44)	1.00	
	Not employed	59 (42.5)	80 (57.5)	2.7(0.731-4.071)	0.010*
Medical and dietary factors					
Presence of GIT disorder	Yes	17 (94.4)	1 (5.6)	0.03(0.04-0.282)	0.242*
	No	56 (38.4)	90 (61.6)	1.00	
Strict vegetarian	Yes	64 (79.1)	17 (20.9)	3.8(1.013-2.077)	<0.001*
	No	9 (10.8)	74 (89.2)	1:00	
Number of meals per day	< 3	46 (79.3)	12 (20.7)	11(5.18-24.249)	<0.001*
	≥ 3	27 (25.5)	79 (74.5)	1:00	
Hemoglobin levels	Low	62 (89.9)	7 (10.1)	0.6(0.005-0.040)	<0.001*
	Normal	11 (11.6)	84 (88.4)	1.00	

GIT=Gastrointestinal disorder, *p<0.2, cOR=crude Odds Ratio, CI=Confidence Interval

Table 3: Multivariable analysis of associated factors of vitamin B12 deficiency among patients with skin hyperpigmentation at AVBRH (n=164).

Variable	Category	cOR(95%CI)	P value	aOR(95%CI)	P value
Socio-demographic factors					
Age in years	10-19	2.3(0.789-6.606)	0.128*	1.2(2.07-4.09)	0.158
	20-29	1.1(0.369-2.737)	0.992	7.1(1.120-2.737)	0.009**
	30-39	2.6(0.510-13.16)	0.118*	0.3(0.001- 6.847)	0.211
	40-50	1.00		1.00	

Continued.

Variable	Category	cOR(95%CI)	P value	aOR(95%CI)	P value
Marital status	Single	2.3(1.069-4.745)	0.033*	1.2(0.169-2.745)	0.414
	Married	6.1(0.623-60.31)	0.120*	6.8(0.623-60.31)	0.757
	Widow	1.00		1.00	
Distance from NHC	≤ 5km	1.00		1.00	
	> 5km	4.4 (0.089-0.347)	<0.001*	3.8 (0.024-0.187)	0.005**
Employment status	Employed	1.00		1.00	
	Not employed	2.7(0.731-4.071)	0.010*	2.5(0.731-4.071)	0.026**
Medical and dietary factors					
Presence of GIT disorder	Yes	0.03(0.04-0.282)	0.242*	0.01(0.03-0.112)	0.520
	No	1.00		1.00	
Strict vegetarian	Yes	3.8(1.013-2.077)	<0.001*	2.1 (0.141-1.050)	0.002**
	No	1:00		1:00	
Number of meals per day	< 3	11(5.18-24.249)	<0.001*	9.1(3.14-7.320)	0.005**
	≥ 3	1:00		1:00	
Hemoglobin levels	Low	0.6(0.005-0.040)	<0.001*	0.2(0.002-0.010)	0.802
	Normal	1.00			

GIT=Gastrointestinal disorder, *p<0.2, **P<0.05, cOR=crude Odds Ratio, aOR =adjusted Odds Ratio, CI=Confidence Interval

DISCUSSION

Mean vitamin B12 deficiency among patients with skin hyperpigmentation

The findings of the study reveal a significant difference in mean plasma vitamin B12 levels between strict vegetarians and non-strict vegetarians attending the dermatology department at Acharya Vinoba Bhave Rural Hospital. The mean plasma vitamin B12 level among strict vegetarians was 201 pg/ml with a standard deviation (SD) of 50.4, and a 95% confidence interval (CI) of 201±10.2 pg/ml. In contrast, the mean plasma vitamin B12 level among non-strict vegetarians was 314 pg/ml with an SD of 91.6, and a 95% CI of 314±16.5 pg/ml.

The observed mean plasma vitamin B12 level of 201 pg/mL among strict vegetarians falls far below the generally accepted normal range for plasma vitamin B12 levels, which is typically between 239-931 pg/ml.¹³ The 95% CI (190.8 to 211.2 pg/ml) suggests that even after accounting for variability within the sample, the upper limit is within the deficiency threshold. This finding is consistent with existing literature, which indicates that strict vegetarians, especially in India where vegetarianism is prevalent, are at a higher risk of vitamin B12 deficiency due to the lack of adequate dietary sources of the vitamin.² Given that vitamin B12 is primarily obtained from animal-derived foods, individuals who follow strict vegetarian diets are at increased risk of developing vitamin B12 deficiency unless they supplement their diet with fortified foods or supplements.¹⁵ The relatively low mean plasma vitamin B12 levels in this group emphasize the need for awareness and proactive measures to address potential deficiencies in this population.

In contrast, the mean plasma vitamin B12 level among non-strict vegetarians was 314 pg/mL, which falls within the normal range. The 95% CI (297.5 to 330.5 pg/ml) further supports that the majority of non-strict vegetarians in this study had sufficient levels of vitamin B12. The higher mean and wider confidence interval in non-strict vegetarians compared to strict vegetarians can be attributed to the inclusion of some animal products in their diet, which serve as rich sources of vitamin B12.¹⁶

The significantly higher plasma vitamin B12 levels in non-strict vegetarians highlight the impact of dietary habits on vitamin B12 status. This finding aligns with previous studies that have shown a clear correlation between the consumption of animal products and adequate vitamin B12 levels.¹⁵ Moreover, the wider range of plasma vitamin B12 levels in non-strict vegetarians, as indicated by the larger SD of 91.6, may reflect varying degrees of adherence to non-vegetarian diets, which can influence individual vitamin B12 status.

Prevalence of vitamin B12 deficiency among patients with skin hyperpigmentation

The study found a prevalence of vitamin B12 deficiency of 44% among 164 respondents attending the dermatology department at Acharya Vinoba Bhave Rural Hospital. This finding is consistent with other studies conducted in similar populations, highlighting the significant public health concern posed by vitamin B12 deficiency in India, particularly among specific dietary groups and those with underlying conditions.

The 44% prevalence of vitamin B12 deficiency observed in this study aligns with the broader epidemiological trends observed in India, where vitamin B12 deficiency is common due to dietary practices and other contributing factors. Previous studies have reported varying prevalence rates depending on the population studied,

with rates ranging from 30% to 70% in different parts of the country.^{3,15} The prevalence of vitamin B12 deficiency among asymptomatic adults is 47%, which closely mirrors the findings of the current study.⁵

The high prevalence of vitamin B12 deficiency in this cohort can be attributed to the predominant dietary habits in the region. In India, a large portion of the population follows vegetarian or vegan diets, which are naturally low in vitamin B12 since this vitamin is primarily found in animal products.¹⁵ Strict vegetarians, in particular, are at increased risk of deficiency, as evidenced by the lower mean plasma vitamin B12 levels discussed earlier. The lack of fortified foods and the limited use of vitamin B12 supplements further exacerbate the risk.¹⁵

In addition to dietary practices, other socioeconomic and health-related factors may contribute to the high prevalence of vitamin B12 deficiency observed in this study. Low socioeconomic status, which limits access to a diverse and nutrient-rich diet, has been identified as a key factor in the development of vitamin B12 deficiency.³ Furthermore, gastrointestinal disorders such as malabsorption syndromes, which are prevalent in certain populations, can impair the absorption of vitamin B12 from the diet, increasing the risk of deficiency.¹³

The findings of this study are particularly relevant for patients with dermatological conditions such as skin hyperpigmentation, where vitamin B12 deficiency may be an underlying or contributing factor. The association between vitamin B12 deficiency and hyperpigmentation has been well-documented, with the deficiency leading to alterations in melanin synthesis and distribution.¹⁷

Associated factors of vitamin B12 deficiency among patients with skin hyperpigmentation

Our study found a significant likelihood of vitamin B12 deficiency among patients with skin hyperpigmentation who were strict vegetarian. they were 2.1-fold likely to have vitamin B12 deficiency (OR=2.1, 95%CI: 0.141-1.050; p=0.002). This observation was in agreement with a study done in India in which inadequate intake of animal source foods was a significant contributed to vitamin B12 deficiency.²

Our findings indicated that patients who had skin hyperpigmentation with reduced number of meals less than 3 per day were 9.1 folds the odds of having low serum vitamin B12 (OR=9.1; 95%CI: 3.14-7.320, p=0.005). This is consistent with findings from United State which mention that people who don't eat enough food are prone to have vitamin B12 deficiency.¹⁸

Our study indicated that, young participants in the age category of 20-29 years were 7.1 times likely to get vitamin B12 deficiency (OR=7.1; 95%CI: 1.120-2.737; p=0.009). This is in agreement with a study in India where young people were more likely to developed

vitamin B12 deficiency probably due to lack of enough intrinsic factor.²

The current study also established an association between distance to nearest health facility and vitamin B2 deficiency. Patients who reside more than 5 kilometers from health facility were 3.8 more likely to have low serum vitamin B12 levels (OR=3.8, 95%CI: 0.024-0.187; p=0.005). Similarly, patients who were not employed were likely to developed vitamin B12 deficiency (OR=2.5, 95%CI: 0.731-4.071; p=0.026)

This study did not establish an association between vitamin B12 deficiency and gastrointestinal disorders such as malabsorption syndrome, crohn disease and pernicious anemia. However other researchers attributed malabsorption syndrome and pernicious anemia to vitamin B12 deficiency due to gastric atrophy in older persons especially among poor populations worldwide in which India is not an exception.²

Since the study involved a cross-sectional approach, it will only provide a snapshot of the relationship between skin hyperpigmentation and Vitamin B12 deficiency at a specific point in time. This limits the ability to establish cause-and-effect relationships. The study was conducted in a specific geographical area (Wardha, India) in a rural hospital setting, meaning the findings might not be generalizable to urban populations or other regions with different healthcare access, diet, and lifestyle factors.

CONCLUSION

The management of colorectal cancer has progressed over the past few decades because of many advances, including those in genetics, pathology, imaging, medical oncology, radiation oncology, and surgery.¹⁶ Undoubtedly, the management of patients afflicted with colorectal cancer will evolve as advances continue to be made in the multiple disciplines that contribute to the diagnosis and treatment of colorectal cancer.

Recommendations

There is a need for routine assessment of vitamin B12 among patients with skin hyperpigmentation at health facilities by the attending clinicians There is a need for health authorities in AVBRH hospital to sensitize the public and healthcare workers on the predictor factors for vitamin B12 deficiency among patients with skin hyperpigmentation to prevent vitamin B12 deficiency cases. For healthcare providers at Acharya Vinoba Bhave Rural Hospital, these findings highlight the importance of considering vitamin B12 deficiency in the differential diagnosis of patients presenting with skin hyperpigmentation or related symptoms. Preventive measures, including dietary education, the use of vitamin B12-fortified foods, and supplementation, should be promoted among at-risk populations. Regular monitoring of vitamin B12 levels by clinicians in high-risk groups

such as strict vegetarian is crucial to prevent the potential complications of deficiency, which can include neurological and hematological disorders

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