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Study of Vitamin B12 Deficiency in Vegetarian Outpatients Presenting to a Tertiary

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Abstract

Vitamin B12 deficiency is a critical public health issue, particularly among vegetarians who are at higher risk due to their diet. This study aimed to explore the prevalence, symptoms, and health implications of Vitamin B12 deficiency among vegetarian outpatients at a tertiary care hospital in Surat, India.

The cross-sectional study included 113 participants aged 18 to 60, who adhered to a vegetarian diet and presented with clinical signs of Vitamin B12 deficiency. A comprehensive clinical evaluation was conducted, and various hematological and biochemical tests were performed, including serum B12 levels.

The results showed that 53.98% of participants had Vitamin B12 deficiency, while 28.32% had borderline levels. Despite the deficiency, 64.6% of participants were non-anemic, indicating that symptoms may manifest even before changes in hemoglobin levels are detectable. Common clinical symptoms included glossitis and peripheral neuropathy, while macrocytes were observed in over 85% of participants' blood smears.

The study highlights the need for early detection and intervention in Vitamin B12 deficiency to prevent severe complications, particularly in vegetarian populations. The findings underscore the importance of supplementation and fortification strategies in regions where vegetarianism is prevalent.

Keywords: NIL

Introduction

Vitamin B12, a crucial water-soluble vitamin, is predominantly found in animal-based foods [1]. Consequently, individuals with low consumption of animal products, such as vegetarians and vegans, are at a heightened risk of deficiency [1,2,3]. This deficiency is of particular concern in India, where vegetarian diets are common making fortification or supplementation essential [4]. Vitamin B12 deficiency can lead to significant health issues, including macrocytic anemia, elevated mean corpuscular volume (MCV), neurological disorders due to impaired myelin sheath production and hyper-homocystenemia which is a significant risk factor for cardiovascular disease [5]. Altered signal conduction leads to paresthesia and subacute combined degeneration of spinal cord where symptoms may range from tingling sensations and glossitis to more severe manifestations such as cognitive impairment and psychosis. The clinical diagnosis of Vitamin B12 deficiency typically involves measuring serum B12 levels, but normal results do not always rule out deficiency. In such cases, serum homocysteine or methylmalonic acid tests can provide additional diagnostic information [5]. This study aims to address the prevalence and implications of Vitamin B12 deficiency among vegetarians in India, exploring its causes, symptoms, and potential health consequences. It also examines current treatment strategies and highlights the need for enhanced awareness and further research. By providing a detailed analysis of

Vitamin B12 deficiency, this research contributes valuable insights to the field and is intended to inform both scholarly and clinical audiences.

METHODOLOGY

One hundred and thirteen patients who presented to department of general medicine out-patient clinic were enrolled in a cross-sectional, observational study from March 2021 to July 2022 at a tertiary care hospital in Surat, Gujarat, India. Patients who had a vegetarian diet and were asymptomatic as well as those who presented with a history of weakness, tiredness, lethargy, tingling and burning sensation in legs, reduced exercise tolerance, forgetfulness, knuckle discoloration, mouth ulcers, anosmia, dysgeusia or difficulty in walking constituted the study population. We also included patients who showed clinical signs like pallor, tachycardia, glossitis, loss of proprioception, hyperreflexia, ataxic gait, positive Romberg's and Lhermitte's signs.

Inclusion criteria: All patients who has a purely vegetarian diet, and/or demonstrated clinical symptoms or signs of Vitamin B12 deficiency in the age group of 18-60 years were included.

Exclusion criteria: All patients who were on Vitamin B12 supplementation, patients on mixed diet (including eggs/fish/chicken/red meat) or those who had undergone any past GI surgery or blood transfusion were excluded from the study. Those patients with systemic diseases, malignancies, dementia and other causes of anemia (Hemolytic, iron deficiency anemia, aplastic anemia, anemia of chronic disease, hemoglobinopathies and other hereditary causes of anemia) were not included. Further, patients who were not willing to participate in the study were excluded.

This study protocol was approved by IECHR (Institute of Ethics Committee for Human Research) with reference no. 39-02/11/2022.

An informed consent was obtained from all patients who were willing to participate in the study. A detailed history including origin, duration and progress of symptoms, treatment history, past history of chronic diseases like diabetes, hypertension, thyroid disorders or infectious conditions like tuberculosis, concurrent medications, dietary habits and obstetric and menstrual history (in females) was elicited from the patient. General and systemic examination was carried out for all patients. Investigations like Complete hemogram, reticulocyte count, serum Vitamin B12 levels, lactate dehydrogenase levels, sickling test, direct and indirect Coombs' test, G6PD deficiency test, urine routine examination with microscopy, liver function tests and renal function tests were carried out for enrolled patients.

All the data was compiled and tabulated in Microsoft Excel. Statistical analysis was performed using chi square tests (categorical variables) and student t test and ANOVA test (continuous data).

RESULTS

Among the study participants, mean age was noted to be 39.9 years with a standard deviation of 12.05. The distribution of males and females was almost equal in the study population (54.9% vs 45.1%). On analyzing the history collected through the proforma, 16.8% patients were betelnut chewers. Elicitation of past history revealed that 10.8% patients had diabetes mellitus, 8.8% patients had hypertension while 10% patients had ischemic heart disease. The treatment history revealed that 12% patients were consuming PPI/H2 blockers, 12% patients were on metformin treatment while 10% were on aspirin treatment.

Glossitis and peripheral neuropathy were present in almost half of the patients (44.2% and 51.3% respectively). On general examination, it was observed that hyperpigmentation (seen in 15% patients) was a more common clinical sign than pallor (noted in 12% patients). Complete hemogram showed that mean hemoglobin level in study populations was 12.54 ± 1.94 gm/dL. According to the indices, average of mean corpuscular volume among all patients was 90.62±17.63. More than three-fourth patients (85.84%) had macrocytes on peripheral smear. Mean value of Vitamin B12 levels in serum was 235.96 ± 123.78 pg/mL. On categorization of patients based on presence of anemia in study population, surprisingly a majority of 73 (64.6%) patients were found to be non-anemic with hemoglobin levels of more than or equal to 12 gm/dL and no patients has severe anemia (hemoglobin levels of less than 8 gm/dL). Seven patients (6.19%) had mild anemia (hemoglobin levels in range of 11-11.9 gm/dL) while 33 (29.21%) patients had moderate anemia (hemoglobin levels in range of 8-10.9 gm/dL). On stratification of patients as per the levels of vitamin B12 in serum, 61 (53.98%) patients were found to be deficient with levels <200 pg/mL, 32

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(28.32%) were borderline deficient with levels in range of 201-300 pg/mL while only 20(17.69%) patients have normal levels of vitamin B12. On analysis, a negative correlation was found between mean corpuscular volume and levels of vitamin B12. However, this was statistically not found to be significant, possibly suggesting that a sub-clinical vitamin B12 deficiency could emerge considerably earlier than detectable changes observed in peripheral blood smears.

DISCUSSION

This cross-sectional study was conducted in 113 vegetarian patients belonging to age group of 18 to 60 years who visited the out-patient clinic of general medicine department at a tertiary level hospital in Surat, Gujarat.

The prevalence of vitamin B_{12} deficiency in vegetarian Indians is found to as high as 70 % [5,6]. Vitamin B_{12} deficiency has been divided into four stages: in stages I and II, indicated by a low plasma level of holo-transcobalamin, the plasma and cell stores become depleted. Stage III is characterized by increased plasma levels of total homocysteine and methylmalonic acid (MMA) along with lowered holo-TC. In stage IV, clinical signs become recognizable such as macro-ovalocytosis, elevated mean corpuscular volume (MCV) or lower hemoglobin levels. Stage III of vitamin B_{12} deficiency has been found in over 60 % of vegetarians [5]. Table 1 gives a brief overview of previous research studies and their findings [3,5,6,7,8].

(TABLE 1)

In our study mean age of study participants in our study was be 39.9 ± 12.05 years. This was in close concordance with study by Patel S.V. et al with mean age of 35.37 ± 14.40 years and Aher A et al with 34.17 ± 12.32 years. The distribution of males and females was almost equal in the study population (54.9% vs 45.1%) with slight male preponderance. A very similar distribution was found in a study by Singh et al [10] with 52.27% males and Anil K Gupta et al., [14] with 44% males and. Another study by Yajnik et al. [6] also corroborated that Vitamin B12 deficiency was higher in Indian men.

Although most cases are clinically subtle, vitamin B12 deficiency may sometimes present with florid disease [10,11]. When present, symptoms and signs can be broadly classified into hematological and neurological categories. Classically, vitamin B12 deficiency may give rise to megaloblastic anemia and sub-acute combined degeneration of the spinal cord with demyelination of the dorsal column, resulting in both motor and sensory deficits. Less commonly, hemolysis and pancytopenia may be detected in the blood work, and neurological sequelae of optic nerve atrophy, autonomic nervous system dysfunction, peripheral neuropathy, as well as psychiatric complications of emotional lability, mania, paranoia, delusions, amnesia and psychosis, may also be present [12] .

In our study, 16.8% patients were betelnut chewers. A study by Iqbal M.P. et al found that the tobacco and betelnut chewing group had significantly lower levels of folate and vitamin B12 compared to the non-user group ($p<0.001$ and $p=0.003$, respectively), however this was not corroborated in our study. Diabetes mellitus was seen in 10.8% patients of our study, Refsum et al [7] demonstrated a significantly higher (54%) of patients suffering from diabetes in the study population.

In our study, 12% patients were consuming PPI/H2 blockers and metformin each. In a study by Patel S.V. et al, no statistically significant association was found between metformin intake and vitamin B12 deficiency. Meanwhile, in a study conducted by Kim et al. (2019) in Korea in type 2 diabetics found out that there was statistically significant association of increasing dose of metformin with vitamin B12 deficiency while there was no association with the duration of consumption of metformin [13]. Ten percent of patients in our study were on aspirin treatment for ischemic heart disease which may have a loose link to hyper-homocystenemia due to vitamin B12 deficiency and associated cardiovascular morbidity.

In our study, glossitis and peripheral neuropathy was present in almost half of the patients (44.2% and 51.3% respectively). According to Singh et al[10], glossitis and peripheral neuropathy were seen in 34.45% and 98.18% patients respectively. Current study showed that hyperpigmentation (seen in 15% patients) was a more common clinical sign than pallor (noted in 12% patients). In a study by Aher A et al., most common sign elicited was pallor in 96% of patients while icterus and knuckle hyperpigmentation

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were present in 57% and 74% of patients, respectively [15]. According to Singh et al[10], hyperpigmentation is found in 16.81% patients which was in concordance with our study.

Mean hemoglobin level in our study populations was 12.54 ± 1.94 gm/dL. These levels were significantly less in a study by Aher A et al. (6.09 ± 2.21 g/dL) and 66% patients had severe anemia which was in complete discordance with our study having 73 (64.6%) patients were found to be non-anemic and no patients has severe anemia. According to Andres et al [11], 37% individuals were having anemia overall. Average of mean corpuscular volume among all patients of our study was 90.62±17.63 fL. Srikanth et al reported an average MCV was 98.47 ± 10.14 fL, which was similar to our study [16]. According to Aaron S et al[17], 17.5% patients had both hemoglobin and the mean corpuscular volume (MCV) within the normal range. In our study 64% patients had hemoglobin in normal range and 14% patients having normal mean corpuscular volume.

More than three-fourth patients (85.84%) had macrocytes on peripheral smear. This was in concordance with study by Aher A et al, having 96% macro-ovalocytes on peripheral smear. Mean value of Vitamin B12 levels in serum was 235.96 ± 123.78 pg/mL. Mean vitamin B12 level in patients was 162.64 ± 43.31 pg/mL. in a study by Aher et al [15]. In our study, negative correlation was found between mean corpuscular volume and levels of vitamin B12. However, this was statistically not found to be significant, possibly suggesting that a sub-clinical vitamin B12 deficiency could be seen much prior to detectable changes observed in peripheral blood smears.

CONCLUSION

Vitamin B12 deficiency is a significant public health concern in India, particularly among vegetarians and individuals with chronic alcohol consumption. The clinical manifestations of this deficiency are diverse and can impact multiple organ systems. Despite its potential severity, both the diagnosis and management of Vitamin B12 deficiency are straightforward and cost-effective. Early detection and intervention are crucial in mitigating the adverse effects of this deficiency, especially in resource-limited settings such as India. Prompt and effective management at the primary care level can prevent the development of severe complications and is economically advantageous.

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TABLES AND FIGURES

TABLE 1

Study	Setting and population	Vitamin B12 levels (median) (pg/ml)	Prevalence of deficiency (%)
Singla et al, 2019, IJEM [3]	524 males and 498 females from urban areas in tier 3 city	351.74	31.40
Naik et al, 2018, BJN [5]	46 males and 73 females from urban area	Males: 198.56 Females: 222.28	Males: 77 Females: 50
Yajnik et al, 2006, JAPI[6]	441 males from rural, slums and urban areas	149.09	67
Refsum et al, 2001, AJCN [7]	63 subjects from urban area	216.86	46

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Study	Setting and population	Vitamin B12 levels (median) (pg/ml)	Prevalence of deficiency (%)
Shobha et al, 2011, IJMR[8]	175 elderly urban subjects from south India	414.74	16

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