STUDY OF RISK FACTORS AND CLINICAL PROFILE OF VITAMIN B12 DEFICIENCY IN GERIATRIC POPULATION.

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ABSTRACT

Background: Vitamin B12 deficiency is a worldwide deficiency disorder. It affects 5-20% of older adults. There is a need to reduce the consequences of vitamin B12 deficiency for which early risk assessment and management. It can affect several organs, such as the bone marrow and the peripheral and central nervous systems. Psychiatric symptoms such as mental and mood disorders, as well as cognitive dysfunction, are also common in people with Vitamin B12 deficiency.

Objectives: To study the risk factors and clinical profile of Vitamin B12 deficiency in the geriatric population.
Methodology: 100 elderly patients were enrolled, and their estimated vitamin B12 levels were measured.
Results: The study included 100 participants (46 females, 54 males) with an average age of 71.89 ± 4.2 years. 76 people reported tiredness, followed by giddiness. 40 had diabetes, and 38 had hypertension as a comorbidity. The mean hemoglobin is 11.66 ± 1.9 g/dL. The mean MCV is 107.59 ± 28.9. Significant association was noticed between tobacco use and hypothyroidism with respect to vitamin B12 levels, and between hemoglobin, MCV, and vitamin B12 levels.
Conclusion: we concluded that not all clinical features of B12 deficiency need to be present simultaneously; hematological findings can be minimal or absent. vitamin B12 levels may be normal in some patients with deficiency symptoms and therefore, we cannot rely on B12 estimation alone. Early initiation of treatment will reverse progressive neurological deterioration in patients with Vitamin B12 Deficiency.

Keywords: Vitamin B12, Geriatric population, Risk factors, Clinical profile, Cognitive dysfunction, Neuropsychiatric symptoms, Megaloblastic anemia, Mean corpuscular volume (MCV), Comorbidities (diabetes, hypertension).

INTRODUCTION

Vitamin B12 deficiency is a worldwide deficiency disorder. Vitamin B-12 deficiency was once thought to occur mainly in people consuming strict vegetarian diets (so it was also known as VEGAN'S DISEASE) and is relatively common, especially among the elderly. Dietary sources of vitamin B12 are foods of animal origin, such as red meat, liver, fish, and dairy products. Insufficient dietary intake of vitamin B12 (<4–5 μg/day) can cause vitamin B12 deficiency. In addition, intestinal absorption of vitamin B12 requires the release of vitamin B12 from food proteins, normal secretion and function of intrinsic factor, and appropriate gastrointestinal acidity. [1] According to the World Health Organization, the geriatric population comprises individuals aged 60 years and above.

Vitamin B12 is utilized in the body for myelin protein synthesis which will help for neurological function, deoxyribonucleic acid synthesis, and red blood cell production. Without appropriate assessment of risk factors, signs, and symptoms, and subsequent management, patients will continue to have a trajectory of continued deficiency leading to chronic complications that are not reversible, leading to lifelong symptoms such as neuropathy, memory loss, dementia, and fatigue. [2]. Vitamin B12 deficiency affects 5-20% of older adults, with up to 40% with low B12 levels [<260 pmol/L]. The risk of B12 deficiency increases with age. Vitamin B12 is essential for neurological function. The causes of vitamin B-12 deficiency in older people are not fully understood, but the consequences can be severe and may include hematological, neurological, and cognitive changes. There is a need to reduce the consequences of vitamin B12 deficiency by doing early risk assessment and management. This helps to improve the earlier evaluation and management of risk factors of vitamin B12 deficiency, before patients develop irreversible symptoms.

Vitamin B12 (cobalamin) deficiency can affect multiple organs, including the bone marrow and the peripheral and central nervous systems [2]. The signs and symptoms of deficiency are variable and mostly nonspecific. Patients often seek help in primary care. Malabsorption of vitamin B12 is the leading cause of clinically manifested vitamin B12 deficiency among adults. Pernicious anemia, atrophic gastritis, and other gastrointestinal conditions can cause B12 malabsorption. People with vitamin B12 deficiency due to malabsorption disorders present with gastrointestinal symptoms (episodes of abdominal distress, distension, nausea, and diarrhea) [1], in addition to symptoms such as neuropathy caused by the deficiency itself [3]. Manifestations of the hematopoietic system, such as megaloblastic anemia, can be diagnosed using readily available laboratory markers. Approximately 30–50% of patients with vitamin B12 deficiency have some degree of neurological involvement [4]. Neurological conditions include myelopathy, like subacute combined degeneration of the spinal cord (SACD). Psychiatric symptoms such as mental and mood disorders and cognitive dysfunction are also common in people with B12 deficiency [3, 4, 5]. If the diagnosis of neuropsychological manifestations of

vitamin B12 deficiency is delayed, symptoms may become irreversible [2,7] within variable time intervals (months to years), depending on residual B12 stores in the liver.
The serum concentration of vitamin B12 is a commonly used marker of vitamin B12 status. The majority of vitamin B12 in blood is bound to haptocorrin, which is not available for B12dependent enzymatic reactions in cells. Holo-transcobalamin is vitamin B12-bound to transcobalamin and consists of a small portion of total serum B12 that is biologically active. Adenosylcobalamin and methylcobalamin insufficiency result in increased plasma concentrations of methylmalonic acid and homocysteine, respectively. Circulating vitamin B12 may not be lowered in all patients with vitamin B12 deficiency [8]. Using metabolic markers of vitamin B12 status, such as methylmalonic acid and homocysteine, to aid in the diagnosis of clinically manifested vitamin B12 deficiency has benefits but also limitations [9], including high measurement costs, limited availability, and the impact of renal insufficiency on concentrations. The severity of vitamin B12 deficiency symptoms at first presentation affects the choice of treatment modality. For example, original parenteral treatment is used when clinical symptoms are severe [10]. For the long-term management of pernicious anemia after vitamin B12 replenishment, parenteral administration with B12 every 1–3 months appears to be sufficient to avoid relapse. Recent studies suggest that the effectiveness of parenteral and high-dose oral vitamin B12 (1 mg/d) in altering serum vitamin B12 concentrations is similar, although the evidence is of low quality. Nevertheless, high-dose oral Vitamin B12 can likely be used for maintenance treatment in many patients [11, 12, 13]. The UK National Institute for Health and Care Excellence (NICE) published guidance principles to facilitate the care of people with vitamin B12 deficiency [14]. However, given uncertainties and a lack of evidence across aspects of the diagnosis and treatment of vitamin B12 deficiency, widely accepted guidelines remain necessary due to between-country differences in medical practices, healthcare systems, and limited resources.

MATERIAL AND METHODS

- **Study Duration**: The study was done for a period of 18 months from June 2022 to January 2024.
- **Source of Data**: Patients attending the outpatient department and inpatient department of the general medicine at Raja Rajeswari Medical College and Hospital, Bangalore, were included.
- **Study Design**: This is an observational hospital-based study done in 100 patients.

- Enrolment: Elderly patients from medical wards were enrolled.

- **Sample Size**: It was estimated that a total of 100 patients were needed for the study n=Z_(1-α/2) ^2 pq/d^2 where,

Z1 - α/2 - value of the normal deviate at the considered level of significance. *p* – expected proportion of the event in the study group, *d* – expected absolute allowable error in the p (10% relative allowable error as 10% of p). Z_(1-α/2) = 1.96 at a confidence interval of 95%

Inclusion criteria

The inclusion criteria comprised patients aged 65 years and above, of either sex, who provided informed consent to participate in the study.

Exclusion criteria

The exclusion criteria included patients admitted to the intensive care unit (ICU), those with debilitating diseases, individuals with a known history of malignancy, and patients receiving parenteral vitamin B12 therapy or regular vitamin B12 or multivitamin supplementation.

Methods of Data Collection

Institutional Ethical Review Board approval was obtained from Raja Rajeswari Medical College and Hospital, Bangalore (Approval No. RRMCH-IEC/56/2023), before initiation of the study. All patients who met the inclusion criteria were enrolled in the study after providing consent and indicating willingness to undergo the required investigations.

The data was captured in the case record form [CRF], which was broadly classified into A. Demographic Characteristics: Name, age, sex, address, contact details, monthly income, languages known, occupation, educational level, rural/urban, religion.

B. Patient history – Medical history, family history, and drug history details were noted
C. Biochemical investigations: CBC, FBS, HBA1C, ECG, serum Vitamin B12, renal function tests, liver function tests, and 2D ECHO were noted.
D. Other investigations – Investigations like upper gastrointestinal endoscopy, upper gastrointestinal biopsy, and intrinsic factor study, nerve conduction study, as and when required, were done.

RESULTS

The data comprise measurements from 100 subjects aged over 65 years.
The following tables provide the details.

Table 1: Distribution of subjects according to age (years) and gender.

Variable	Subcategory	Number of subjects (%)
Age (years)	65-70	41 (41%)
	71-75	32 (32%)
	76-80	27 (27%)
	Mean ± SD Median (Min, Max)	71.89 ± 4.2 71.5 (65, 80)

The mean age was 71.89 ± 4.2 years. Out of 100 (100%) subjects, 41 (41%) were in the age group 65-70 years, 32 (32%) subjects were in the 71-75 age group, and 27 (27%) subjects were in the 76-80 age group. 46% were females and 54% were males.

Table 2: Distribution of Gender of the study population

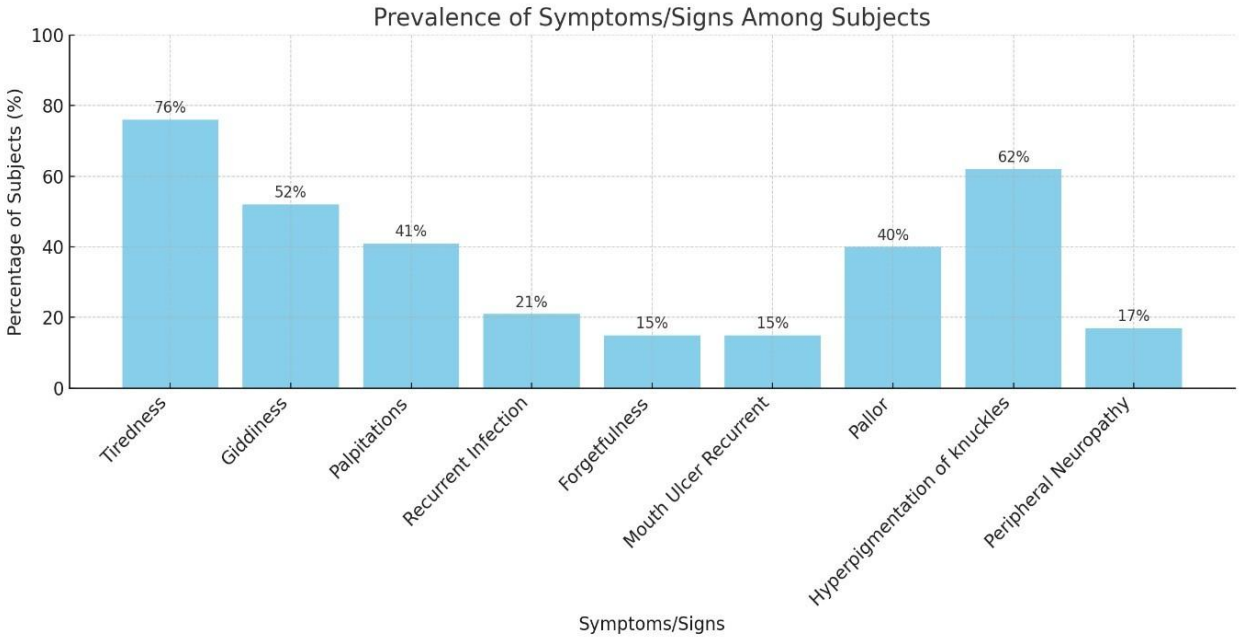
Gender	N (%)
Male	54 (54%)
Female	46 (46%)

Table 3: Distribution of subjects according to symptoms and clinical signs

Variable	Number of subjects (%)
Tiredness	76 (76%)
Hyperpigmentation of knuckles	62 (62%)
Giddiness	52 (52%)
Palpitations	41 (41%)
Pallor	40 (40%)
Recurrent Infection	21 (21%)
Peripheral Neuropathy	17 (17%)
Forgetfulness	15 (15%)
Mouth Ulcer Recurrent	15 (15%)

With respect to the distribution of subjects across variables, 76 (76%) had tiredness, 52 (52%) had giddiness, 41 (41%) had palpitations, 21 (21%) had recurrent infections, and 15 (15%) had forgetfulness.

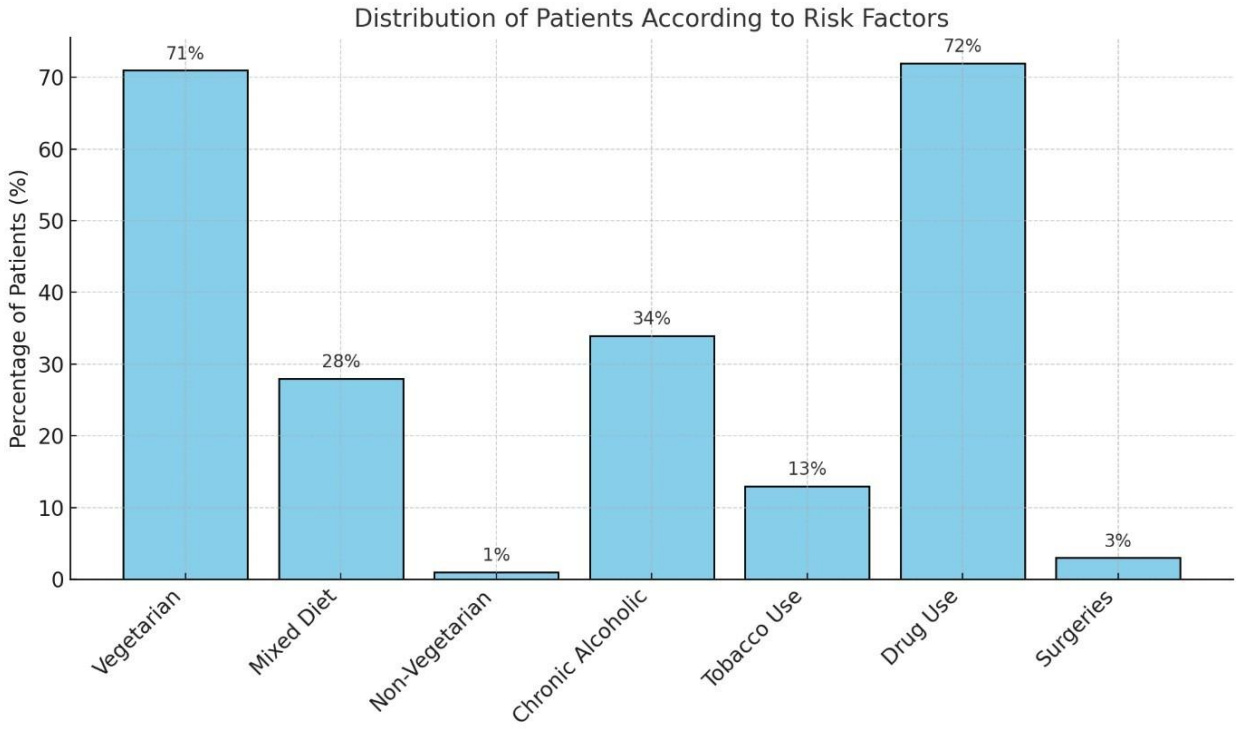
Graph 1: Distribution of the subjects based on the symptoms and signs



Distribution of patients according to risk factors:

34% were chronic alcoholics, and 13 (13%) of the subjects were consuming tobacco. Most of the subjects were vegetarians.

Graph 2: Distribution of patients according to habits and food patterns



Distribution of comorbid conditions

On analyzing the co-morbidities, 40 (40%) had diabetes, and 38 (38%) had hypertension.

Graph 3: Distribution of comorbid conditions

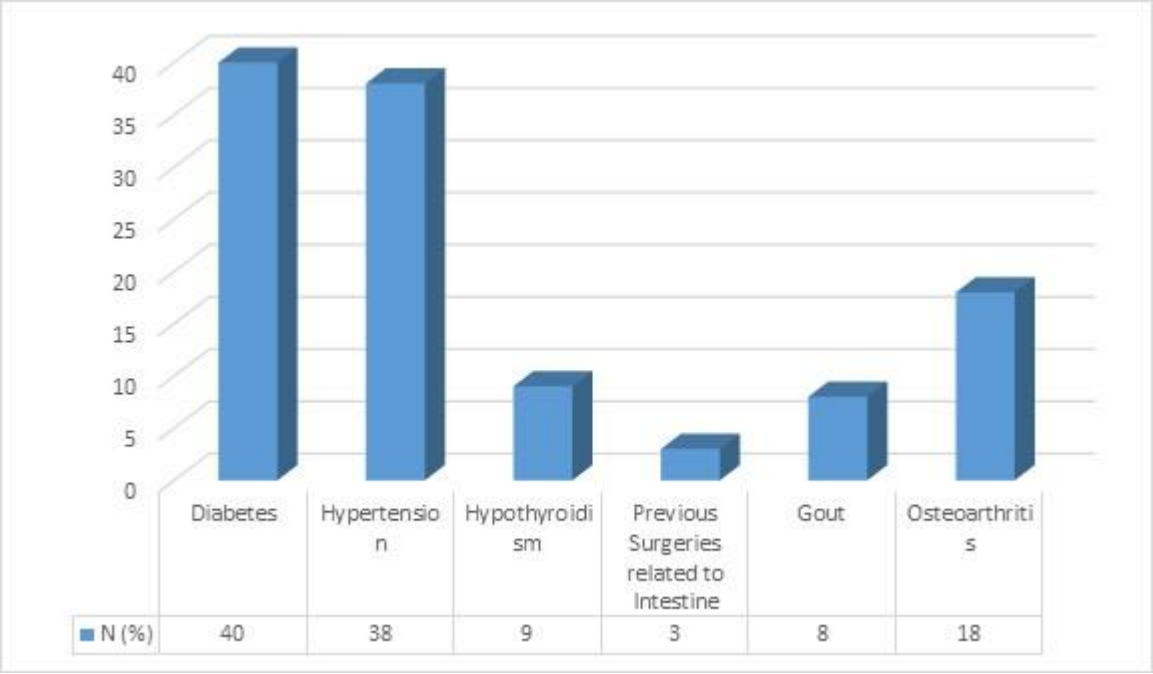


Table 4: Distribution of average MMSE and Incidence of peripheral neuropathy

Peripheral Neuropathy	No	83 (83%)
	Yes	17 (17%)
MMSE Score	Mean ± SD Median (Min, max)	27.08 ± 2.49 28 (22, 30)

Graph 4: Distribution of subjects based on peripheral smear.

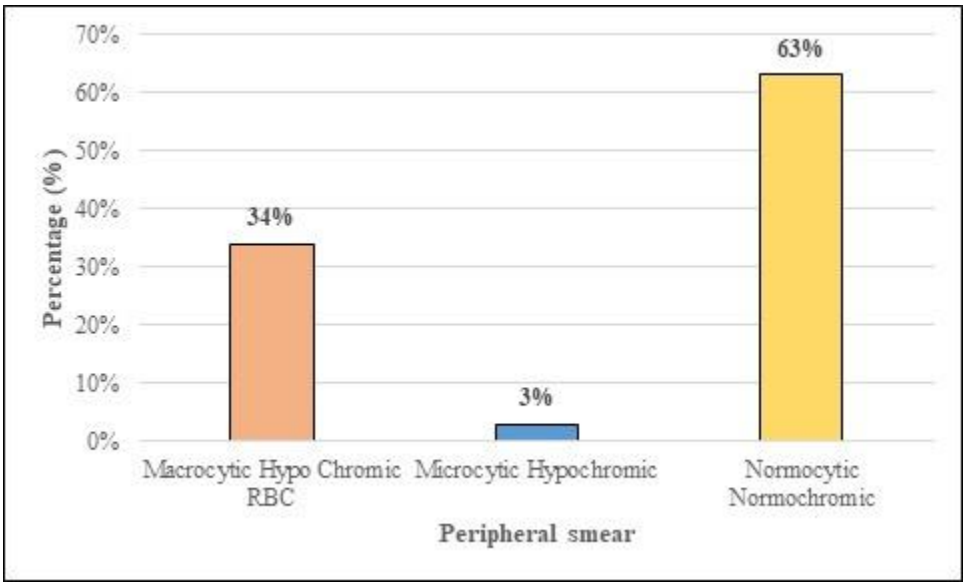


Table 5: Distribution of subjects according to hematological parameters and vitamin B12.

Variable	Subcategory	Study parameters (%)
Hemoglobin (g/dL)	Mean ± SD Median (Min, Max)	11.66 ± 1.9 12.5 (8.1, 14)
MCV	Mean ± SD Median (Min, Max)	107.59 ± 28.9 95.7 (72.6, 177.78)
Peripheral Smear	Normocytic Normochromic	63 (63%)
	Macrocytic Hypo Chromic RBC	34 (34%)
	Microcytic Hypochromic	3 (3%)
Vitamin B12	>180	66 (66%)

	<180	34 (34%)
	Mean ± SD Median (Min, Max)	143 ± 24.51 153.7 (90.6, 167.9)
Hyper segmented	Present	51 (51%)
	Absent	49 (49%)
Neutrophils		

The mean hemoglobin is 11.66 ± 1.9 g/dL. The mean MCV is 107.59 ± 28.9. Out of 100 (100%) subjects, 63 (63%) peripheral smears were normocytic normochromic. The mean vitamin B12 was 143 ± 24.51. Of 100 (100%) subjects, 66 (66%) had a vitamin level greater than 180.

Graph 5: Distribution of subjects based on Vitamin B12.

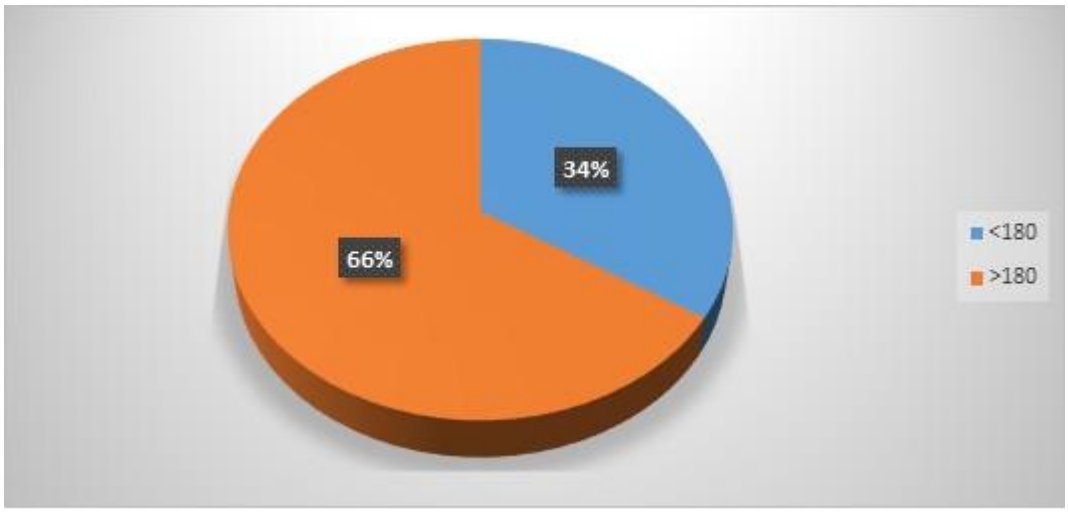


Table 6: Distribution of subjects according to medication intake

Variable	Number of subjects (%)
PPI	26 (26%)
Metformin	22 (22%)
Steroids	19 (19%)
Methotrexate	3 (3%)
Antipsychotics	2 (2%)

With respect to medication use, 22 (22%) subjects were on metformin, 19 (19%) on steroids, and 26 (26%) on PPI.

Table 7: Distribution of subjects according to duration of drug therapy in years.

Variable	Subcategory	Duration of drug therapy (%)
Duration of ongoing Drug Therapy (years)#	Mean ± SD Median (Min, Max)	6.85 ± 4.23 8 (1, 16)

The mean duration of ongoing Drug Therapy was 6.85 ± 4.23 years.

Graph 6: Mean plot of Hemoglobin over Vitamin B12.

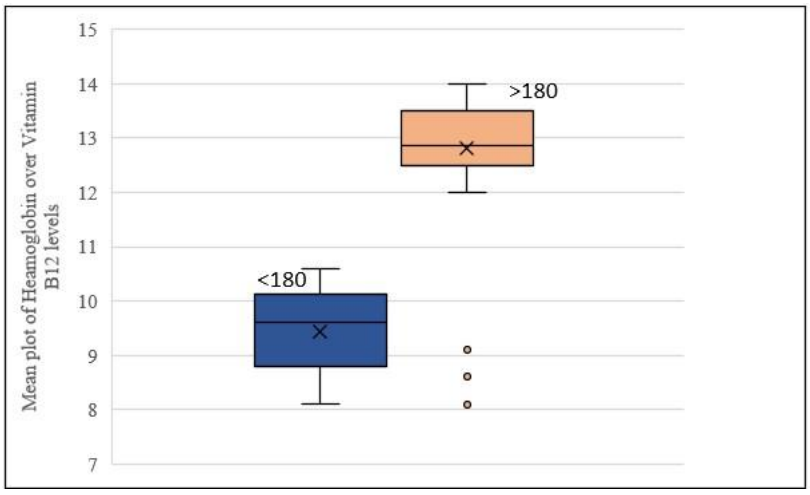


Table 8: Distribution of subjects according to different variables in relation to Vitamin B12 levels

Subcategory	Vitamin B12	
	<180	>180

Variable		Number of subjects (%)		p-value
	65-70	13 (38.2%)	28 (42.4%)	
Age (years)	71-75	12 (35.3%)	20 (30.3%)	0.871[C]
	76-80	9 (26.5%)	18 (27.3%)	
Gender	Female	17 (50%)	29 (43.9%)	0.564[C]
	Males	17 (50%)	37 (56.1%)	
Tiredness	Yes	30 (76.5%)	46 (63.6%)	
	No	8 (23.5%)	24 (36.4%)	0.192[C]
Giddiness	Yes	17 (50%)	35 (53%)	
	No	17 (50%)	31 (47%)	0.773[C]
Palpitation	Yes	12 (35.3%)	29 (43.9%)	
	No	22 (64.7%)	37 (56.1%)	0.405[C]
Recurrent infection	Yes	8 (23.5%)	13 (19.7%)	
	No	26 (76.5%)	53 (80.3%)	0.655[C]
Forgetfulness	Yes	6 (17.6%)	9 (13.6%)	
Mouth ulcer	No	28 (82.4%)	57 (86.4%)	0.594[C]
recurrent	Yes	6 (17.6%)	9 (13.6%)	
Peripheral	No	28 (82.4%)	57 (86.4%)	

Neuropathy	Yes	5 (14.7%)	12 (18.2%)	0.594[C]
	No	29 (85.3%)	54 (81.8%)	
Pallor	Yes	15 (44.1%)	25 (37.9%)	0.661[C]
	No	19 (55.9%)	41 (62.1%)	
Chronic Alcoholic	Yes	11(32.4%)	23(34.8%)	0.546[C]
	No	23 (67.6%)	43 (65.2%)	
Tobacco	Yes	1 (2.9%)	12 (18.2%)	0.802[c]
	No	33 (97.1%)	54 (81.8%)	
Diabetes	Yes	14 (41.2%)	26 (39.4%)	0.031[C]
				0.863[C]
	No	20 (58.8%)	40 (60.6%)	
Hypertension	Yes	14 (41.2%)	24 (36.4%)	0.638[C]
	No	20 (58.8%)	42 (63.6%)	
Food habits	Mixed	7 (20.6%)	21 (31.8%)	0.360[C]
	Non-Veg	0	1 (1.5%)	
	Veg	27 (79.4%)	44 (66.7%)	
Other Comorbidities	Gout	2 (5.9%)	6 (9.1%)	0.672[C]
	Nil	26 (76.5%)	52 (78.8%)	
	Osteoarthritis	6 (17.6%)	8 (12.1%)	
Hypothyroidism	Yes	6 (17.6%)	3 (4.5%)	**0.030[C]**
	No	28 (82.4%)	63 (95.5%)	
Previous surgeries related to intestine				0.225[C]

Yes	2 (5.9%)	1 (1.5%)
No	32(94.1%)	65(98.5%)

*Abbreviation: Chi-square test; * indicates statistical significance*

On analysing, using the Chi-square test, it can be observed that there is a significant association between tobacco use and hypothyroidism with respect to Vitamin B12 levels.

Graph 7: Mean plot of MCV over Vitamin B12 levels.

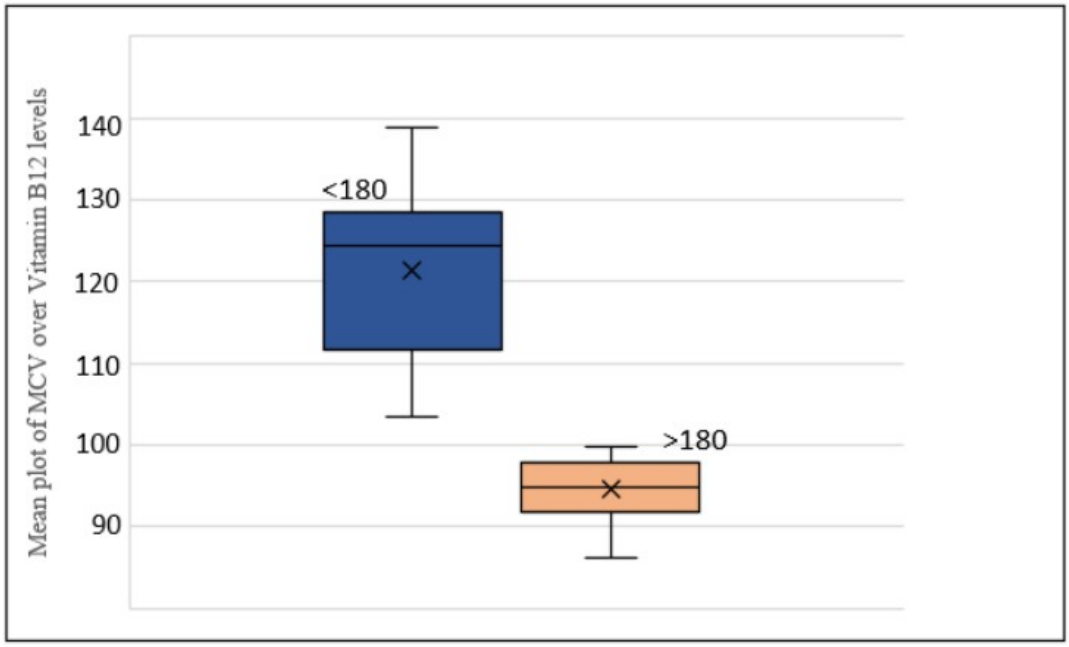


Table 9: Distribution of subjects according to Vitamin B12 levels in relation to hemoglobin and MCV

Variable	**Subcategory**	**Vitamin B12**		**p-value**
		<180	**>180**	
Hemoglobin	Mean ± SD Median (Min,	**Number of subjects (%)**		**<0.001*MW**

	Max)	9.4 ± 0.8 9.6 (8.1, 10.6)	12.8 ± 1.1 12.9 (8.1, 14)	
MCV	Mean ± SD Median (Min, Max)	142.89 ± 21.79 148.79 (107.1, 177.78)	89.14 ± 6.61 89.75 (72.6, 99.7)	**<0.001*[MW]**

*Abbreviation: MW- Mann-Whitney U test, *- indicates statistical significance*

Vitamin B12 levels were analysed using the Mann-Whitney U test. It was observed that there is a significant difference in the means of Hemoglobin and MCV over Vitamin B12 levels.

Table 10: Association of Vit B12 levels with concomitant use of medications.

Variable	**Sub-category**	**Vitamin B12**		**p-value**
		<180	**>180**	
		Number of subjects (%)		
Metformin	Yes	9 (26.5%)	13 (19.7%)	0.438[C]
	No	25 (73.5%)	53 (80.3%)	
Methotrexate	Yes	0	3 (4.5%)	
	No	34 (100%)	63 (95.5%)	
Steroids	Yes	6 (17.6%)	13 (19.7%)	0.804[C]
	No	28 (82.4%)	53 (80.3%)	
Antipsychotics	Yes	1 (2.9%)	1 (1.5%)	0.629[C]
	No	33 (97.1%)	65 (98.5%)	
PPI	Yes	9 (26.5%)	17 (25.8%)	0.938[C]
	No	25 (73.5%)	49 (74.2%)	

DISCUSSION

Vitamin B12 deficiency is a worldwide deficiency disorder. The causes of vitamin B-12 deficiency in older adults are not fully understood, but the consequences can be severe and include hematological, neurological, and cognitive changes. There is a need to decrease the consequences of Vitamin B12 Deficiency for Early Risk Assessment and Management. Malabsorption of vitamin B12 is the main cause of clinically manifested vitamin B12 deficiency among adults. Pernicious anemia, atrophic gastritis, and other gastrointestinal diseases can cause B12 malabsorption. [1]

In this study, the risk factors, co-morbidities, and clinical profile of Vitamin B12 were studied in the geriatric population. A total of 100 patients were examined for risk factors, and the clinical profile of Vitamin B12 was analysed. In our study, Vitamin B12 <180 was considered deficient according to our lab reference values and the machine's validation. The mean age group was 71.89 ± 4.2 years. Out of 100 subjects, 41 (41%) were in the age group 65-70 years, 32 (32%) subjects were in the 71-75 age group, and 27 (27%) subjects were in the 76-80 age group. 46% were females and 54% were males. Our study results were like of Singh et al. [15], who reported a maximum of 27.27% of cases in the 55-70-year age group, with 52.27% being males. The results of Manoj Kumar et al. [16] were also in line with ours, as they reported that 16% of their study subjects were in the 60-79-year age group. In their study, females accounted for the largest share, at 57%.

All 100 subjects were asked to report risk factors, including signs and symptoms, habits, and comorbid conditions. The MMSE score was also recorded, with a mean of 27.08 ± 2.49. Around 51% reported hypersegmented neutrophils. We noted that the majority in our study complained of tiredness (76%), followed by hyperpigmentation of the knuckles (62%), giddiness, and palpitation (52% and 41%, respectively). Moore et al. [17] reported similar results, with 65% of their subjects complaining of fatigue. Patel et al. [18] also reported that fatigue was the most common symptom among their subjects.

Smoking can cause a deficiency in vitamin B12 and other micronutrients. This is because cigarette smoke depletes vitamins in the body [15]. Only 13% reported tobacco use, which was significantly associated with Vitamin B12 deficiency. Studies conducted by Singh et al., Khan et al., and Harsh Arora et al. [15,19,20] concluded that among patients who smoked, vitamin B12 deficiency was significantly higher than in those who did not smoke ($p < 0.001$).

With respect to the comorbid conditions, 40% had diabetes, followed by hypertension. This was similar to the study conducted by Singh et al. [15] in our study, a statistically significant association was seen between hypothyroidism and Vitamin B12 deficiency. This was in relation to the study by Singh et al., which reported that 8.63% of patients with hypothyroidism had Vitamin B12 deficiency. A similar study by Jabbar et al. [22] in Karachi reported a 40% prevalence of Vitamin B12 deficiency among hypothyroid patients.

Bacteria synthesize vitamin B12, and its root source is the consumption of animal-derived products such as meat, eggs, and dairy products, but not in plant-derived products. Most of the subjects in our study were vegetarians. Ramesh et al. [23] concluded that Vitamin B12 deficiency was common in both vegetarians and non-vegetarians and reported that 46% of the subjects were vegetarians, a proportion like our study results. While some studies conducted by Qazi et al. and Jatoi et al. [24,25] revealed that the major causes of vitamin deficiency are inadequate consumption of animal-source foods and pernicious anemia in the young population. At the same time, malabsorption in part of the gut due to gastric atrophy may be the leading cause of the deficiency state in older patients.

In our study, 51 (51%) of subjects had hyper segmented neutrophils on peripheral blood smears. These results from our study were similar to those reported by Singh et al. [15], which accounted for 60% of their cases. Our data also supported the study by Briani et al. [25], which investigated cobalamin deficiency using clinical examination and radiological findings. Up to 17% of patients with vitamin B12 deficiency reported peripheral neuropathy. A study by Briani et al. [25] reported similar results, noting that 76% of patients' pathological findings showed axonal degeneration with or without demyelination. Another study conducted by Singh et al. [15] revealed that 57.89% of their patients had neuropathy.

Depression, apathy, irritability, dementia, catatonia, delirium, and hallucinations were well reported in the study conducted by Jayaram et al. [27] MMSE score from our study showed a mean range of 27.08 ± 2.49. This was similar to the study results of Singh et al. [15]. Other studies conducted by Eastley et al [28] confirmed that mild depression among 6.36% of patients with vitamin B12 deficiency, and they also recovered with vitamin B12 supplementation.

Hematological manifestations result from inadequate vitamin B12, leading to ineffective DNA synthesis and impaired erythropoiesis. In India, folate deficiency is an equally important cause of megaloblastic anemia. Combined B12 and folic acid deficiency is more common than B12 or folic acid deficiency alone, and 45% of non-anemic individuals have either a subnormal level of B12 alone or combined B12-Folate Deficiency. In our study, the mean Haemoglobin is 11.66 ± 1.9 g/dL. Studies conducted by Singh et al [15] and Andres et al [10] reported severe anemia, defined as Hb levels < 7 g/dL, in 23.18% and > 6 g/dL in 37% of their patients, respectively. Their study results were in contradiction with our study, in which none of our participants had such low Hb levels. The study results by Moore et al. [17] were close to our study, which was < 10.1 g/dL. In general, B12 and folic acid deficiencies are suspected when MCV is more than 100 fl. In our study, the mean MCV is 107.59 ± 28.9 and out of 100 (100%) subjects, 63 (63%) peripheral smears had Normocytic Normochromic, which was like study results of Moore et al. [17] Very rarely some patients with profound cobalamin deficiency does not even have higher MCV values which could be due to concomitant iron deficiency, thalassemia trait or anemia of chronic disease.

Vitamin B12 deficiency causes a moderate-to-severe anemia with a slow onset; patients may have few symptoms relative to the degree of anemia. In our study, the mean Vitamin B12 level was 143 ± 24.51 pg/ml, and 66% of subjects had >180 pg/ml. This was in relation to the study

results by Singh et al. [15]. Vitamin B12 supplementation before a hospital visit can affect serum B12 levels. During vitamin B12 depletion, it falls first in neuronal tissues and is reflected in the serum much later.

One more thing to emphasize is that self-medication is common in India, and the study traced 26% of cases who were taking PPI/ H2 blockers. This is another challenging issue contributing to vitamin B12 deficiency. Conversely, a study by Qorraj et al. [29] conducted in 250 adult subjects who used PPIs for 12 months did not show clinically significant vitamin B12 deficiency. The study encountered comorbidities, as many individual patients were suffering from more than one disorder. Here, the study revealed that 22% of diabetes cases were on metformin ± other antidiabetic drugs. The mean duration of ongoing drug therapy was 6.85 ± 4.23 years. Singh et al. [15] reported similar results in their study. Metformin itself is a common cause of vitamin B12 deficiency among drugs. Therefore, patients on metformin for a long time need close monitoring for vitamin B12 deficiency, or B12 supplementation in patients at higher risk.

This study explores the diversity of clinical presentations, the risk population, and how a clinical condition can be treated easily if the diagnosis is confirmed. Better understanding the clinical spectrum of Vitamin B12 deficiency is critical for Primary care clinicians and can also be used as a clinical aid to identify Vitamin B12 deficiency.

CONCLUSION

Based on our study and analysis, vitamin B12 deficiency can present in various forms. Early recognition is paramount to prevent irreversible neurological damage. Therefore, a high index of suspicion should be maintained in patients presenting with cutaneous and/or neuropsychiatric symptoms, particularly among strict vegetarians, the elderly population, and those refractory to conventional treatment. A bone marrow examination may be essential when the complete hemogram and serum vitamin B12 levels are normal. An MCV greater than 90 FL, in an appropriate clinical setting, may suggest vitamin B12 deficiency. Not all clinical features of vitamin B12 deficiency need to be present simultaneously.

Hematological findings may be minimal or absent; in some patients, vitamin B12 levels may appear normal, and thus, B12 estimation alone is insufficient for diagnosis. Early initiation of treatment can reverse progressive neurological decline in patients with vitamin B12 deficiency. We conclude that undiagnosed vitamin B12 deficiency is widespread. This suggests that, in current clinical practice, laboratory testing is often triggered only by overt signs and symptoms. Routine screening may enable earlier diagnosis and reduce associated morbidity.

However, long-term trials are required to evaluate the benefits of treating asymptomatic individuals. No specific risk groups among older adults can be clearly defined, although advancing age itself increases the likelihood of vitamin B12 deficiency. Therefore, routine screening should be considered for individuals aged 65 years and above. We propose measuring total vitamin B12 as the first-line test, with a cutoff of <180 pg/mL to confirm deficiency and >910 pg/mL to rule it out. Additional measurements, such as homocysteine and holotranscobalamin, are recommended for individuals with borderline vitamin B12 levels (180–

910 pg/mL). However, variations in local reference ranges limit the establishment of uniform diagnostic criteria.

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