

Identifying Typical Presentations of Vitamin B-12 Deficiency among Individuals Attending Tertiary Care Hospital in Central Gujarat: A Case Control Study

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Abstract:

Introduction: Vitamin B12 is mainly obtained through non vegetarian diet, milk and milk products. Malabsorption and inadequate intake leads to haematological and neurological disorders. **Objective:** To determine the symptoms and signs associated with Vitamin B12 deficiency. **Method:** A case control study was conducted at the medicine department of tertiary care hospital. Patients visiting hospital with serum Vitamin B12 level below 200pg/ml were labelled as cases and more than 200 pg/ml were labelled as controls, irrespective of signs and symptoms of Vitamin B 12 deficiency. Controls were matched for age to minimize confounding. 160 cases and 160 controls were selected. Pretested semi structured questionnaire was used to identify signs and symptoms of Vitamin B12 deficiency among cases and controls. Chi square test was applied for each symptom between cases and control, of which 10 were significant ($p < 0.05$). ROC curve was plotted for the 10 symptoms to check their usefulness for diagnosing vitamin B12 deficiency. **Results:** Area-Under Curve (AUC) was maximum under knuckle pigmentation (0.794), (Positive Likelihood Ratio (PLR)=3.24) followed by poor memory (0.684), (PLR=3.25) tingling and numbness (0.624), (PLR=1.84) and dizziness (0.605), (PLR=1.38) in respective order. Whereas fatigue, sore and swollen tongue, pale skin, breathlessness, palpitation, insomnia, memory loss were not associated with Vitamin B12 deficiency ($p > 0.05$). **Conclusion:** Presence of knuckle pigmentation, poor memory, tingling and numbness, and dizziness can be defined as hallmarks of Vitamin B12 deficiency and can be used to predict and start Vitamin B12 supplementation.


Keywords: Diagnostic algorithm, India, Tertiary hospital, Vitamin B-12 deficiency

Introduction:

Vitamin B12 is required in the production of red blood cells for their healthy cell growth and repair; its deficiency causes anaemia, which is manifested by easy fatigability, weakness, loss of appetite and weight loss. It also has vital role in the synthesis of DNA, the genetic material, as well as necessary for myelin formation, in combination with folic acid, thus

maintaining neurological system. In the absence of Vitamin B12 abnormalities develops characterised by impaired memory, tingling and numbness in finger and toes. It also presents with disorientation, frequent mood changes, irritability, depression, sometimes leading to dementia and psychosis.^[1]

Cyanocobalamin deficiency is one of the commonest deficiencies and is associated with

Quick Response Code	Access this article online	How to cite this article : Patel S, Makwana A, Gandhi A, Chugh L, Bhavsar V. Identifying Typical Presentations of Vitamin B-12 Deficiency among Individuals Attending Tertiary Care Hospital in Central Gujarat: A Case Control Study. Healthline. 2024; 15 (1): 31-39
	Website : www.healthlinejournal.org	
	DOI : 10.51957/Healthline_590_2024	

hematologic, neurologic, psychiatric, cutaneous, gastrointestinal, and cardiovascular diseases, and it impacts individuals of all ages. As diet is the only main source of Vitamin B12, its malabsorption and inadequate intake leads to haematological and neurological disorders building a public health problem worldwide.^[2] The prevalence of vitamin B12 deficiency is estimated to be 47% in India^[3] which is significantly more as compared to 15-20% of elderly in the United States are B12 deficient.^[4]

The recommended dietary allowance (RDA) for Vitamin B12 is 2.2mcg/day in men and women aged 14 years and above. Most Vitamin B12 is obtained through ingestion of meat, liver, kidney, fish, chicken, egg, milk, curd, cheese, and the body stores remain for years.^[5]

Person suffering from Vitamin B12 deficiency develops megaloblastic anaemia, a clinical condition characterized by abnormalities in red blood cells. Advance cases present with neurological abnormalities and sometimes psychiatric symptoms.^[6]

Variable haematological, neuropsychiatric, and mucocutaneous abnormalities can be signs of vitamin B12 deficiency. Knuckle hyperpigmentation associated with vitamin B12 insufficiency has been seen, however typically these individuals present with systemic symptoms as megaloblastic anaemia, pancytopenia, or neurological impairments. It further emphasises how critical it is to identify this cutaneous symptom as an early indicator of vitamin B12 insufficiency, allowing the doctor to address the patient's condition before it results in severe brain consequences.^[7]

Absence of Serum Vitamin B12 testing facilities at PHC and Sub-center levels, and at many district levels, sparked the motivation for this study. Through analyzing ROC curves and p-values, our aim is to anticipate signs and symptoms of Vitamin B12 deficiency and determine the feasibility of initiating treatment without blood tests at the periphery level. Present study was conducted to determine the

signs and symptoms associated with Vitamin B12 deficiency.

Method:

The study was conducted after ethical clearance from *IECHR* (Institutional Ethical Committee for Human Research).

A case control study was conducted at a tertiary care hospital from November 2017 to June 2018. Cases were selected from medicine department of the hospital based on the serum Vitamin B12 level, less than 200pg/ml irrespective of the signs and symptoms of Vitamin B12 deficiency.^[7] Controls were defined as those patients visiting the medicine department with serum B12 level above 200pg/ml. Irrespective of the signs and symptoms of Vitamin B12 deficiency. Controls were matched with cases as per age group to minimize confounding.

Information was collected from both cases as well as controls during their hospital visits to medicine department. Written consent was taken prior to interviews, and information related to health effects due to Vitamin B12 deficiency like Sore swollen tongue, Dizziness, Tingling & Numbness, Difficulty in concentrating or poor memory, Indigestion, diarrhoea, constipation and Bloating, Weight loss, Cool extremities, Symptoms of fatigue, Insomnia, difficulty in walking and headache associated with Vitamin B12 deficiency were collected by using pretested semi structured questionnaire.^[6] An attempt was made to look for symptoms and signs associated with the level of Vitamin B12. Individuals who had taken parental or oral Vitamin B12 within last six months and patients operated for gastrectomy, ileal malabsorption, Crohn's disease, ileal resection, and diagnosed tapeworm infestation were excluded from the study.

A pilot study was conducted on 15 cases and 15 controls in tertiary care hospital, Vadodara to generate the data for calculation of sample size. By using OpenEpi software, 95% CI, 90% power, Type I error 5%, ratio of cases to controls 1:1, percentage of

tingling and numbness among controls as 30%, and expected odds ratio for tingling and numbness as 2.2, sample size came out to be 155 in each group. So we have taken 160 cases and 160 controls for conducting case control study.

Cases and controls were matched by five years age group (Frequency matching). The process of data collection did not pose any potential risk or harm to the participants. Data safety and confidentiality was given due consideration by keeping the file containing identity related details password protected PID and the filled proforma was kept in lock and key accessible only to the researchers. Data was entered in Epicollect 5, extracted in Excel 2007 sheet, and was analysed using Epi InfoTM 7 software. Chi square test was applied to check for association between symptoms and Vitamin B12 deficiency ($p < 0.05$) and odds ratio was calculated. ROC curve was plotted for those symptoms which were statistically significant by chi square to check their usefulness for diagnosing vitamin B12 deficiency.

Results:

Table 1 shows Socio demographic profile of the participants among cases and controls.

As mentioned in Table 2, knuckle pigmentation (OR=8.15, 95% CI=4.92 to 13.51, $p = < 0.001$), Dizziness (OR=1.83, 95% CI=1.18 to 2.81, $p=0.007$), tingling and numbness (OR=2.70, 95% CI=1.70 to 4.30, $p < 0.001$) Indigestion/ diarrhoea/ constipation and bloating (OR=2.05, 95% CI=1.16 to 3.61, $p=0.013$), weight loss (OR=2.03, 95% CI=1.18 to 3.69, $p=0.02$), cool extremities (OR=2.41, 95% CI=1.01 to 5.71, $p=0.046$), M.C.V ≥ 100 (OR=3.78, 95% CI=2.11 to 6.75, $p = < 0.001$), Headache (OR=1.81, 95% CI=1.09 to 3.033, $p=0.022$), Difficulty in walking (OR=2.87, 95% CI=1.65 to 4.98, $p < 0.001$) were significantly associated with Vitamin B12 deficiency.

Fatigue, sore and swollen tongue, pale skin, breathlessness, palpitation, insomnia, memory loss was not statistically associated with Vitamin B12 deficiency ($p > 0.05$ at 95% CI).

ROC curve analysis of the diagnostic tests of Vitamin B12 deficiency

The ROC curve used to estimate the accuracy of Knuckle pigmentation, poor memory or difficulty in concentration, tingling and numbness and dizziness as a diagnostic test.

The best predictor of Vitamin B12 deficiency was Knuckle pigmentation. For Knuckle pigmentation an area under the curve (AUC) was 0.794 (SE 0.026, 95% CI: 0.75-0.84), Significance level: $P < 0.001$). An AUC of 0.79 (with a statistical significance of less than 0.05) means that is a good diagnostic test for B12 deficiency. Positive Likelihood ratio of knuckle pigmentation is 3.24. (Figure 1)

For tingling and numbness, we found an area under the curve of 0.624 (SE: 0.03, 95% CI: 0.57-0.68. Significance level: $P < 0.001$). An AUC of 0.62 (with a statistical significance of less than 0.05) means that tingling and numbness a good predictor test for B12 deficiency. Positive Likelihood ratio of tingling and numbness is 1.84. (Figure 1)

Poor memory or difficulty in concentration was also a good predictor of Vitamin B12 deficiency. For poor memory or difficulty in concentration we found an area under the curve of 0.68 (SE 0.07, 95% CI: 0.63-0.73, Significance level: $P < 0.01$). An AUC of 0.68 (with a statistical significance of less than 0.05) means that poor memory or difficulty in concentration is a good diagnostic test for B12 deficiency. Positive Likelihood ratio of that poor memory is 3.25. Poor memory or difficulty in concentration is followed by tingling and numbness, which is also a good predictor of Vitamin B12 deficiency. (Figure 1)

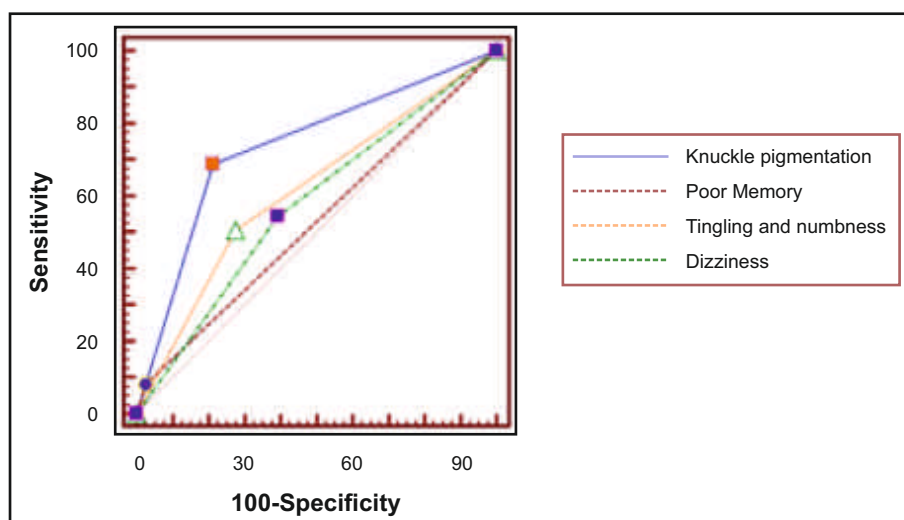
Table 1: Socio demographic profile of the Cases and Controls (N=320)

Variable	Cases (N=160)	Controls (N=160)	p value
	n(%)	n(%)	
Age(years)			
19-28	69 (43.12)	69 (43.12)	1
29-48	61 (38.12)	61(38.12)	
49 and above	30 (18.75)	30 (18.75)	
Mean age (SD)	35.37 (14.40)	35.33 (14.21)	-
Median age (IQR)	32.50 (23.50-45.00)	32.50 (23.50-45.50)	-
Gender			
Male	103 (64.4)	92 (57.5)	0.25
Female	57 (35.6)	68 (42.5)	
Religion			
Hindu	153 (95.6)	148 (92.5)	0.21
Muslim	6 (3.8)	12 (7.5)	
Jain	1(0.6)	0	
Occupation			
Professional	7 (4.4)	2(1.3)	<0.01
Semi-professional	6 (3.8)	2 (1.3)	
Clerical worker	11 (6.9)	6 (3.8)	
Skilled worker	17 (10.6)	6 (3.8)	
Semi-skilled worker	17 (10.6)	10 (6.3)	
Unskilled worker	32 (20.0)	34 (21.3)	
Unemployed	70 (43.8)	100 (62.5)	
Socioeconomic classification*			
Upper class	19 (11.9)	3 (1.9)	<0.001
Upper middle class	11 (6.9)	5 (3.1)	
Middle class	25 (15.6)	17 (10.6)	
Lower middle class	47 (29.4)	61 (38.1)	
Lower class	58 (36.3)	74 (46.3)	
Area of Residence			
Urban	71 (44.4)	45 (28.1)	<0.01
Rural	89 (55.62)	115 (71.9)	
Diet			
Vegetarian	39 (24.4)	18 (11.3)	<0.01
Other than Vegetarian	121(75.6)	142 (88.7)	

* Modified B.G.Prasad's socioeconomic classification-2018

Table 2: Distribution of participants according to various Symptoms of Vitamin B 12 deficiency and their comparison in cases and controls (N=320)

Variables	Cases n(%)	Controls n(%)	OR (95 % CI)	P value
Tingling and Numbness				
Yes	81 (50.6)	44 (27.5)	2.70	<0.001
No	79 (49.4%)	116 (72.5)	(1.70 to 4.30)	
Difficulty in concentrating				
Yes	13 (8.1)	4 (2.5)	3.44	0.034
No	147 (91.9)	156 (97.5)	(1.09 to 10.81)	
Dizziness				
Yes	87 (54.4)	63 (39.4)	1.83	0.007
No	73 (45.6)	97 (60.6)	(1.18 to 2.81)	
Indigestion, diarrhoea, constipationand Bloating				
Yes	41 (25.6)	23 (14.4)	2.05	0.013
No	119 (74.4)	137 (85.6)	(1.16 to 3.61)	
Weight loss				
Yes	36 (22.5)	20 (12.5)	2.03	0.02
No	124 (77.5)	140 (87.5)	(1.18 to 3.69)	
Cool extremities				
Yes	18 (11.3)	8 (5.0)	2.41	0.046
No	142 (88.8)	152 (95.0)	(1.01 to 5.71)	
Difficulty in walking				
Yes	52 (32.5)	23 (14.4)	2.87	<0.001
No	108 (67.5)	137 (85.6)	(1.65 to 4.98)	
Headache				
Yes	50 (31.3)	32 (20.0)	1.8182	0.022
No	110 (68.8)	128 (80.0)	(1.09 to 3.0329)	
Knuckle pigmentation				
Yes	110 (68.8)	34(21.3)	8.15	< 0.001
No	50 (31.3)	126 (78.8)	(4.92 to 13.51)	
Mean corpuscular volume				
≥100	54 (33.75)	19(11.88)	3.78	< 0.001
<100	106 (66.25)	141 (88.12)	(2.11 to 6.75)	

Figure 1: Comparison of ROC curves for Vitamin B12 deficiency

*The dotted line indicates a test with no predictive power (AUC: 0.5).

ROC curve showing the sensitivity and specificity of dizziness for the diagnosis of Vitamin B12 deficiency. The dotted line indicates a test with no predictive power (AUC: 0.5).

Dizziness had the lowest area under the curve; 0.60 (SE 0.03, 95% CI: 0.55-0.66, Significance level: $P < 0.001$). Dizziness is a fair predictor for Vitamin B12 deficiency. Positive Likelihood ratio of that dizziness is 1.38. (Figure 1)

Discussion:

Vitamin B12 is an important factor in metabolic pathway that produces myelin which surrounds the nerves in form of protection and insulation. Vitamin B12 deficiency causes nerve damage as a result of which tingling and numbness in hands and feet is a common symptom. For the purpose of estimating the accuracy of diagnostic ability of symptoms such as knuckle pigmentation, poor memory or difficulty in concentration, tingling and numbness and dizziness, ROC curve was plotted.

ROC curve showing the sensitivity and specificity of knuckle pigmentation, poor memory or difficulty in concentration, tingling and numbness and dizziness for the diagnosis of Vitamin B12 deficiency. Fatigue, sore and swollen tongue, pale skin, breathlessness, palpitation, insomnia, memory loss was not associated with Vitamin B12 deficiency ($p > 0.05$ at 95% CI).

In present study, it was found that tingling and numbness was present 50.6% among cases while 27.5% among controls. The difference was statistically significant at 95% confidence interval. One study found that about 28% of people had neurological symptoms of Vitamin B12 deficiency, without any signs of anaemia.^[8,9]

Statistically significant difference was present for dizziness among cases (54.4%) and controls (39.4%) at 95% confidence interval (OR=1.83, CI= 1.17 to 2.81, $P < 0.01$).

Vitamin B12 deficiency affect nervous system so balance and co-ordination also affected. Making more prone to difficulty in walking and falling.

In present study, it was found that difficulty in walking was present 32.5% among cases while 14.4% among controls. The difference was statistically significant at 95% confidence interval (OR=2.87, CI= 1.65 to 4.98, $P < 0.01$). Anaemia caused by Vitamin B12 deficiency can lead to feeling of breathlessness and dizziness. This occurs because body cannot get enough oxygen to all body cells sufficiently. A case study conducted by Ekabe et al.^[10] revealed that complaints such as progressive burning painful sensations on the upper trunk, paraesthesia, and numbness of the upper and lower limbs were improved by oral therapy with Vitamin B12.

In present study, it was found that difficulty in concentrating or poor memory was present 8.1% among cases while 2.5% among controls. The difference was statistically significant at 95% confidence interval (OR=3.45, CI= 1.10 to 10.82, P=0.034). In a cross sectional study conducted in neurology department of Pakistan by ShaziaJatoi et al.^[11] in 2020 showed that 18.3% of the subjects had poor memory.

J. David Spence^[12] in his review article described that grey matter atrophy and cognitive decline was slowed by B12 therapy. As Vitamin B12 deficiency is commonly prevalent, often missed, and simply treated, it can reduce the risk of stroke and cognitive decline.

Arora et al^[13] study concluded that a high prevalence of Vitamin D/B12 deficiencies among urban populations complaining pain of lower limb and have generalized weakness.

In Vitamin B12 deficiency tongue changes colour and shape, making it painful, red and swollen. Statistically significant difference was not found for sore and swollen tongue among cases (6.9%) and controls (6.9 %) at 95% confidence interval (OR=1, CI= 0.42 to 2.38, P= 1). Studies had shown that a swollen and inflamed tongue that has long straight lesions on it could be an early sign of Vitamin B12 deficiency.^[14]

In present study, it was found that experience of cool extremities was present 11.3% among cases while 5% among controls. The difference was statistically significant at 95% confidence interval (OR=2.40, CI= 1.01 to 5.71, P=0.046).

In present study, it was found that headache was present 31.3% among cases while 20.0% among controls. The difference was statistically significant at 95% confidence interval (OR=1.81, CI= 1.09 to 3.03, P=0.02).

B12 deficiency can manifest in various neuromuscular and gastrointestinal complaints.

Peripheral neuropathy, glossitis, and gastrointestinal disturbances such as diarrhoea are commonly reported symptoms. Additionally, individuals may present with headaches and neuropsychiatric disturbances, reflecting the impact of B12 deficiency on neurological function.^[15]

In present study, it was found that knuckle pigmentation was present 68.8% among cases while 21.3% among controls. The difference was statistically significant at 95% confidence interval (OR=8.15, CI= 4.91 to 13.51, P<0.01)

Srivastava et al^[7] discovered well-demarcated areas of pigmentation localized to the knuckles of both hands in a 29-year-old female on a strictly vegetarian diet. After two months of Vitamin B12 oral therapy, the pigmentation began to regress.

Statistically significant difference was found for 33.75% cases with mean corpuscular volume more than 100 and 11.88 % controls at 95% confidence interval (OR=3.78, CI= 2.12 to 6.75, P< 0.01).

In this study it was observed that knuckle pigmentation is the best predictor of Vitamin B12 deficiency, with area under the ROC curve of 0.794, followed by Poor memory or difficulty in concentration with area under the ROC curve of 0.684 and tingling and numbness with area under the ROC curve of 0.624. Dizziness had the lowest area under the ROC curve of 0.605. Dizziness is a fair predictor for Vitamin B12 deficiency.

Yajnik C.S. et al,^[16] isolated adolescents with Vitamin B12 deficiency and administered an approved physiological dose of 2mg/day for 11 months and demonstrated improvement in pseudomotor function in feet by 14.7%, sensory conduction velocity in median and sural nerves by 16.2% and 29.4% respectively. In their study supplementation of physiological dose helps tackle widely prevalent vitamin B12 deficiency in Indian population with inadequate dietary intake.^[16] The objective of study was to know the symptoms associated with Vit B12 deficiency, but further study is required to see the effect of physiological vitamin

B12, or therapeutic sublingual tablets or injectable vitamin B12 on the deficiency.

In this study symptoms like fatigue and difficulty in walking showed no association with Vitamin B12 deficiency. No association found in depression, insomnia, cool extremities and memory loss. Age, sex, religion and diet were possible confounders in our study. Body doesn't have enough Vitamin B12 to make red blood cells, which transport oxygen throughout your body. Vitamin B12 deficiency can lead to fatigue. This happens because body cannot get enough oxygen in the all cells of body sufficiently.

As per authors knowledge, there is limited literature available on this topic. Since we excluded the other possible causes of Vitamin B12 deficiency such as patients operated for gastrectomy, ileal malabsorption, Crohn's disease, ileal resection, and diagnosed tapeworm infestation; this becomes the strength of our study. But we did not measure homocysteine levels and methylmalonic acid and since the study is conducted in a tertiary care hospital, this is the limitation of our study and further field-based studies with a larger sample size are required.

Screening of Vitamin B12 deficiency based on the common signs and symptoms such as knuckle pigmentation, tingling and numbness and dizziness as found in this study may be useful where Vitamin B12 estimation is not feasible or cost effective. Community based screening and there by early diagnosis of Vitamin B12 deficiency may prevent neurological manifestations. Studies may be undertaken with regards to community-based screening based on common sign and symptoms found in this study.

Conclusion:

The most common symptoms associated with Vitamin B12 deficiency were tingling and numbness, poor memory, dizziness and the most common sign associated with Vitamin B12 deficiency was knuckle pigmentation.

Recommendation:

People with knuckle pigmentation, poor memory, tingling and numbness or dizziness should consume foods fortified with Vitamin B12 or oral or parenteral Vitamin B12 supplementation.

Declaration:

Funding: Nil

Conflict of Interest: Nil

References:

1. Briani C, Torre CD, Citton V, Manara R, Pompanin S, Binotto G, et al. Cobalamin deficiency: Clinical picture and radiological findings. *Nutrients*. 2013;5(11):4521–39. PMID: 24248213 PMCID: PMC3847746 DOI: 10.3390/nu5114521
2. Singh J, Dinkar A, Gupta P, Atam V. Vitamin B12 deficiency in northern India tertiary care: Prevalence, risk factors and clinical characteristics. *J Family Med Prim Care*. 2022 Jun;11(6):2381-2388. doi: 10.4103/jfmpc.jfmpc_650_21. Epub 2022 Jun 30. PMID: 36119310; PMCID: PMC9480660.
3. Singla R, Garg A, Surana V, Aggarwal S, Gupta G, Singla S. Vitamin B12 Deficiency is Endemic in Indian Population: A Perspective from North India. *Indian J Endocrinol Metab* [Internet]. 2019 [cited 2023 May 1];23(2):211. Available from: /pmc/articles/PMC6540890/
4. Eastley R, Wilcock GK, Bucks RS. Vitamin B12 deficiency in dementia and cognitive impairment: The effects of treatment on neuropsychological function. *Int J Geriatr Psychiatry*. 2000;15(3):226–33. doi: 10.1002/(sici)1099-1166(200003)15:3<226::aid-gps98>3.0.co;2-k. PMID: 10713580.
5. ICMR-NIN. ICMR-NIN expert group on Nutrient requirement for Indians, Recommended Dietary Allowances (RDA) and Estimated Average Requirements (EAR) [Internet]. 2020. Available from: https://www.nin.res.in/RDA_short_Report_2020.html
6. Wolffenbuttel BHR, Wouters HJCM, Heiner-Fokkema MR, van der Klauw MM. The Many Faces of Cobalamin (Vitamin B12) Deficiency. *Mayo Clin Proc Innov Qual Outcomes* [Internet]. 2019;3(2):200–14. Available from: <https://doi.org/10.1016/j.mayocpiqo.2019.03.002>
7. Srivastava A, Choudhary S. Knuckle Pigmentation as an Early Cutaneous Sign of Vitamin B12 Deficiency: A Case Report. *JNMA J Nepal Med Assoc* [Internet]. 2020 Oct 1 [cited 2023 May 1];58(230):798. Available from: /pmc/articles/PMC7654476/
8. Nawaz A, Khattak NN, Khan MS, Nangyal H, Sabri S, Shakir M. Deficiency of vitamin B12 and its relation with neurological disorders: a critical review. *J Basic Appl Zool*. 2020;81(1)10 (2020). Available from: <https://doi.org/10.1186/s41936-020-00148-0>

9. Serin HM, Arslan EA. Neurological symptoms of vitamin b12 deficiency: Analysis of pediatric patients. *Acta Clin Croat*. 2019;58(2):295–302. PMID: 31819326; PMCID: PMC6884369.
10. Ekabe CJ, Kehbila J, Abanda MH, Kadia BM, Sama CB, Monekosso GL. Vitamin B12 deficiency neuropathy; a rare diagnosis in young adults: a case report. *BMC Res Notes*. 2017 Jan 28;10(1):72. doi: 10.1186/s13104-017-2393-3. PMID: 28129784; PMCID: PMC5273828.
11. Jatoi S, Hafeez DA, Riaz SU, Ali A, Ghauri MI, Zehra M. Low Vitamin B12 Levels: An Underestimated Cause Of Minimal Cognitive Impairment And Dementia. *Cureus*. 2020;12(2). DOI: 10.7759/cureus.6976 PMID: 32206454 PMCID: PMC7077099
12. Spence JD. Metabolic vitamin B12 deficiency: A missed opportunity to prevent dementia and stroke. *Nutr Res* [Internet]. 2016;36(2):109–16. Available from: <http://dx.doi.org/10.1016/j.nutres.2015.10.003>
13. Arora H, Srivastava N, Bala K. Prevalence of vitamin D/B12 deficiency among urban populations complaining pain of lower limb and generalize weakness. *Asian J Pharm Clin Res*. 2016;9(3):82–4. Available from: <https://journals.innovareacademics.in/index.php/ajpcr/article/view/11194>.
14. Stoopler ET, Kuperstein AS. Glossitis secondary to vitamin B12 deficiency anemia. *CMAJ*. 2013 Sep 3;185(12):E582. doi: 10.1503/cmaj.120970. Epub 2013 Jan 28. PMID: 23359038; PMCID: PMC3761039.
15. Ankar A, Kumar A. Vitamin B12 Deficiency. [Updated 2022 Oct 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK441923/>
16. Yajnik CS, Behere R V, Bhat DS, Memane N, Raut D, Ladkat R, et al. A physiological dose of oral Vitamin B-12 improves hematological, biochemical-metabolic indices and peripheral nerve function in B-12 deficient Indian adolescent women. *PLoS One*. 2019;14(10):8–15. Available from: <https://doi.org/10.1371/journal.pone.0223000>