

A STUDY OF VARIOUS CLINICAL FEATURES MANIFESTED DUE TO THE DEFICIENCY OF VITAMIN B12 INCLUDING DETAILED NEUROLOGICAL AND HAEMATOLOGICAL FEATURES

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ABSTRACT: BACKGROUND: Vitamin B12 (Cobalamin) plays an important role in DNA synthesis and neurologic function. Deficiency can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by early diagnosis and prompt treatment. **MATERIAL AND METHODS:** Cross sectional descriptive study carried out in Medicine department, SMIMER, Surat during the period from June 2009 to December 2010. 30 patients whose Serum Vitamin B12 level <250 pg/ml were included. **RESULT:** The most common complaint was fatigue present in 29(96.7%) followed by anorexia, present in 19(63.3%) patients. Anemia was observed in 25(83.3%) patients. Out of this 25 patients with anemia 13(52%) patients had leucopenia, and 15(60%) patients had thrombocytopenia (platelet count<150000/cumm), while 10 (40%) patient had normal platelet count. 13(52%) out of 25 anemic patients had MCV of 80-100 fl, while 11(44%) had MCV more than 100 fl. 15 patients had neurological features, myeloneuropathy (4 patients) and neurocognitive disorder with neuropathy(4 patients) were the commonest feature. **CONCLUSION:** In patients with Vitamin B12 deficiency anorexia and fatigue are most common symptoms even in absence of anaemia. Anaemia can be associated with normal or high MCV. Pancytopenia is a common feature. The most common neurological presentations were neuropathy and neuropsychiatric involvement.

KEY WORDS: Vitamin B12, Haematological features, Neuropathy, Neuropsychiatric involvement

INTRODUCTION: Vitamin B12 is a member of the vitamin B complex. It is exclusively synthesized by bacteria and is found primarily in meat, eggs and dairy products. The deficiency of this vitamin can occur in strict vegetarians who do not consume even milk and other dairy products. However, defective absorption of vitamin B12 is far more common cause of deficiency than dietary deficiency of this vitamin. Vitamin B12 (Cobalamin) plays an important role in DNA synthesis and neurologic function. Deficiency can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by early diagnosis and prompt treatment.¹

MATERIAL AND METHODS: This was a cross sectional descriptive study carried out in Medicine department, Surat Municipal Institute of Medical Research (SMIMER), Surat during the period from June 2009 to December 2010. Patients having anaemia, neurological features such as motor weakness, ataxia, paraesthesias, chronic headache or other psychiatric symptoms or any of the thrombo-embolic manifestations were screened for their serum vitamin B12 level and patients with serum Vitamin B12 level <250 pg/ml were included in the study. 30 such patients were selected who were either admitted to medicine ward or were attending outpatient department.

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Complaints on presentation, detailed general and systemic examination and all investigations were noted on a predesigned proforma. Each patient had undergone a battery of investigations which included CBC and RBC indices. The serum Vitamin B12 level was measured by flow cytometry method (a non radio isotopic assay) in all patients. Test to rule out other causes of anaemia such as stool for occult blood, Coomb's test, sickling test, G-6 PD and lactate dehydrogenase (LDH) and reticulocyte count (RC) was done in each patient having anaemia. Patients having haemoglobin <11 gm % were considered anaemic and further investigated to rule out other common causes of anaemia and for further haematological parameters.

RESULTS: The most common complaint we observed was fatigue. It was present in 29(96.7%) followed by anorexia, which was present in 19(63.3%) patients. While the least observed symptoms were diarrhea seen only in 1(3.33%) of the patients. Details of the clinical features of Vitamin B12 deficient patients are shown in Table no. 1. Commonest hematological feature observed in our study was anemia which was observed in 25(83.3%) patients out of 30 patients. Severe anemia i.e. haemoglobin value < 7 gm% was equally distributed in various subgroups of vitamin B12 levels. Haemoglobin values and its comparison with Serum Vitamin B12 levels in patients with Vitamin B12 deficiency included in our study are shown in Table no. 2. There were 13(52%) patients having leucopenia (WBC count < 4000/cumm) while only 1 patient had leucocytosis. There were 15(60%) patients having thrombocytopenia (platelet count<150000/cumm) while 10(40%) patient had normal platelet count. There were 12(36%) patients out of 30 patients who had Pancytopenia. In our study 13(52%) out of 25 anemic patients had MCV of 80-100 fl while 11(44%) had MCV more than 100 fl. MCV (fl) values and its comparison with Serum Vitamin B12 levels in patients with Vitamin B12 deficiency included in our study are shown in Table no. 3. In our study 15 patients had neurological features, myeloneuropathy (4 patients) and neurocognitive disorder with neuropathy(4 patients) were the commonest feature, distribution of various neurological features in patients with Vitamin B12 deficiency is shown in Table no. 4.

DISCUSSION: 30 patients with serum Vitamin B12 levels less than 250 pg/cumm were included in the study and their various clinical presentations including neurological manifestations were noted analyzed and compared with the data from other similar case studies.

In our study pallor was found in 19(63.3%) of the patients as the commonest clinical feature as against Nafil reported it in 93.33% of his patients.² Fatigue was the commonest presenting symptom in 96.6% our patients but Healton reported it in only 50% of his patients. We observed anorexia in 19(63.33%) against 143(50%) reported by Healton et al³. In our as well as Healton's study 33.33% patients presented with fever. Third commonest presenting feature in our study was paresthesia 12(40%) against 33% reported by Healton and 12.82% reported by Kakonkar et al⁴. We observed weakness and ataxia in 16.7% of patients while Healton reported it in 12% and Kankonkar reported it in 61.54% of patients in his study. We observed headache as presenting symptom in 33.33% against only 3% reported by Healton et al³.

Hematological features observed by us were mostly comparable to those in other similar studies. We observed Anaemia in 83.3% of patients, while O. Karaman et al⁵ in 96.8% and S Affenberger⁶ reported anemia in 37% of their patients. We observed Pancytopenia in 44% of patients while Nafil et al² observed it in 17.3%, Affenberger in 5% and Maamar et al⁷ in 30.7% of

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their patients. In our study the mean MCV was 98 ± 12 fl, which was similar to Affenberger study (98.9 ± 25.6 fl), while mean MCV reported by Nafil et al was 109fl. Raised MCV was noticed in 44% of our patients, while Affenberger reported it in 54% of his patients. We observed thrombocytopenia in 60% of our patients while Nafil et al observed it in 28%, O. karaman et al in 9% and Affenberger in 9.9% of their patients. The high incidence of thrombocytopenia observed by us might be due to the criteria (< 150000) we considered. Leucopenia was observed by us in 52% of our patients while Nafil et al in 29% and Affenberger in 13.9% of their patients only. Mean Hb in our study was 7.2 ± 3.6 , in Maamar's study it is 6.2 ± 2.6 and 9.3 ± 2.9 in O. karaman study.^{2,5-7}

Neurological presentation, in our study 6.6% patients had spasticity in upper limbs while 33.33% had it in lower limbs. Misra & Kalita reported lower limb spasticity in 13(76.4%) patients while upper limbs were affected in 2(11.7%) patients. In present study 15(33.33%) of the patients had weakness in the lower limbs while J.Kalita reported it in 38.89% of his patients. Joint position & sense of vibration was impaired in 40% of our patients while same was reported in 97.22% by J. Kalita and in 100% by Misra & Kalita.⁸ Peripheral neuropathy was observed by us in 40% of our patients while Chuadhary reported it in 18% and Aaron reported it in only 9% of his patients.^{9,10} Horizontal sensory levels could be established in 13.3% of our patients as against 5.55% reported by Kalita. Knee jerk was exaggerated in 33.33% of our patients while J. Kalita observed it in 77.77% and Heulton in 50%. We observed absence of knee jerk in 6.67% of our patients as against 16.67% reported by J. Kalita. Ankle jerk was exaggerated in 6.67% of our patients while it was absent in 40% as against 57.77% absent ankle jerk reported by J Kalita and 50% by Heulton.^{3,8}

Myeloneuropathy & neurocognitive involvement both were observed in 4 (26.67%) patients. Mishra et al⁸ reported myelopathy in 8 patients and myeloneuropathy in 5 (29.4%) and Heulton et al reported Myloneuropathy in 41% of their patients.^{3,8} In our study no patient had pure Myelopathy but Puri et al⁹ reported it in 5(12.5%) of their patients. Myloneuropathy otherwise was observed in 54% by Aaron et al¹⁰ and in 31(77.5%) of patients by Puri et al. Incidentally we had 01 (6.67%) patient who had cerebellar involvement along with neuropathy. 8% of our patients had neurocognitive disorder and all of them had features in the form of diffuse headache, lack of concentration, irritability, and mood instability. whereas Mishra et al in a similar study observed these findings in 13.8% of patients in 2007. In our study along with myeloneuropathy we observed cognitive involvement in 4 (26.67%) of patients, while Hilton observed it in 8% of his patients and Aaron in 38% of his patients. In our study we didn't find any case of dementia. while in a similar study, it was found in 17.6% of patients by Mishra et al, 10 % of patients by Choudhary and 18% of patients by Aaron.^{3,8,10,11}

CONCLUSION: In patients with Vitamin B12 deficiency anorexia and fatigue are most common symptoms even in absence of anaemia. Anaemia can be associated with normal or high MCV. Pancytopenia is a common feature. The most common neurological presentation are neuropathy and neuropsychiatric involvement followed by myeloneuropathy. Pure myelopathy is relatively rare. The exact pathomechanism of constitutional symptoms and psychiatric involvement is not understood yet and requires further studies.

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TABLES:

Clinical Features	Frequency (n)	Percent (%)
Fatigue	29	96.7
Anorexia	19	63.3
Pallor	19	63.3
Skin pigmentation	15	50.0
Dyspnoea	14	46.7
Paraesthesias in lower limbs	12	40.0

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Fever	10	33.3
Nausea/vomiting	10	33.3
Headache	10	33.3
Glossitis and Stomatitis	09	30.0
Oedema	09	30.0
Psychiatric Symptoms	08	26.7
Paraesthesias In upper limbs	07	23.3
Palpitation	05	16.7
Ataxia	05	16.7
Motor weakness in lower limb	05	16.7
Yellowish discoloration of sclera & urine	04	13.3
Tingling of tongue	04	10.3
Weight loss	03	10
Diarrhoea	01	3.3
Bowel & bladder involvement	01	3.3

Table no. 1: Presenting clinical features of patients with Vitamin B12 deficiency

Hemoglobin (gm %)	Serum Vitamin B12 levels(pg/ml)				Total
	50-100	100-150	150-200	200-250	
<7	5(20)%	5(20)%	4(16)%	1(4)%	15(60)%
7 to 9	0	3(12)%	1(4)%	0	4(16)%
9 to 11	1(4)%	2(8)%	3(12)%	0	6(24)%
Total	6(24)%	10(40)%	8(32)%	1(4)%	25(100)%

Table no. 2: Levels of haemoglobin values and its comparison with Serum Vitamin B12 levels in patients with Vitamin B12 deficiency

MCV(fl)	Serum Vitamin B12 levels(pg/ml)				Total
	50-100	100-150	150-200	200-250	
<80	00	00	01(04%)	00	01(04%)
80 to 100	04(16%)	04(16%)	04(16%)	01(04%)	13(52)%
100 to 110	02(08)%	03(12)%	01(04%)	00	06(24)%
110 to 120	00	03(12)%	02(08)%	00	05(20)%
Total	06(24)%	10(40)%	08(32)%	01(04)%	25(100)%

Table no. 3: Levels of MCV(fl) values and its comparison with Serum Vitamin B12 levels in patients with Vitamin B12 deficiency

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Neurological Features	Frequency (n) %
Myelopathy	00
Myeloneuropathy	04(26.67%)
Neuropathy	02(13.3 %)
Neurocognitive	03(20.00%)
Neurocognitive with myeloneuropathy	01(06.66%)
Neurocognitive with neuropathy	04(26.67%)
Cerebellar disease with neuropathy	01(06.66%)
Total	15(100%)

Table no. 4: Neurological features in patients with Vitamin B12 deficiency

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