

Hematological Parameters versus Serum Vitamin B12 Levels in the Diagnosis of Vitamin B12 Deficiency Neurological Deficits

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Abstract: Vitamin B12 is an important substrate for various enzymes that act as a co factor (adenosylcobalamin) in the conversion of methyl malonyl coA to succinyl coA. Deficiency of vitamin b12 causes the accumulation of methylmalonyl co A as well as impaired dna synthesis leading to impaired myelin production and impaired oligodendrocyte growth and can affect any part of neuroaxis with involvement of other systems as well. Vitamin b12 deficiency causes megaloblastic (dimorphic) anemia that manifests as raised mcv and reduced hemoglobin. Present study concentrates on correlation between this hematological parameters like mcv, hemoglobin, b12 levels and clinical symptomatology of myelopathy, neuropathy or myeloneuropathy. The study determines that estimation mcv and hemoglobin are not sufficient enough to correlate the symptoms as patient may still have low serum b12 levels despite normal mcv and hemoglobin the determination of which is important as it's a potentially treatable disorder if treated at earliest. It determines that there is poor correlation between the clinical symptoms and estimation of hemoglobin and mcv and requires estimation of serum b12 levels for definitive diagnosis.

Keywords: Vitamin B12, MCV, Hemoglobin, myelopathy, neuropathy, myeloneuropathy

1. Introduction

Vitamin B 12 deficiency presents with varied neurological manifestations. It can affect all age groups and both sexes. Different studies have reported different prevalence rates. Most often commonly seen in the older adults and pure vegetarians. Studies also have shown that Vitamin B12 deficiency can affect any part of nervous system and manifest as abnormalities in cognition, spinal cord, peripheral nervous system in the form of behavioural disturbances, memory disturbances, paresthesias, absent joint position sense and other motor abnormalities respectively that could be part of spinal cord or peripheral nervous system. The present study compares the neurological abnormalities in relation to hematological parameters.

Vitamin B-12 or cobalamin (Cbl) is required for the methylation of myelin, neurotransmitters, and membrane phospholipids and is essential for the integrity of the central and peripheral nervous systems^[1,2] Past reviews of cobalamin deficiency highlight diagnostic approaches to this disorder and the presence of a "subtle" preclinical deficiency state.^[3-6] Recent studies suggest unique biochemical and physiologic actions of Cbl and limitations in diagnostic testing. The present study shows the limitations of the hematological parameters like MCV and Hb in the assessment of these vitamin B 12 deficiency patients and its poor correlation to clinical abnormalities.

Vitamin B 12 deficiency and its neurological manifestations are reversible if detected early and treated. Hence it is important to know the sensitivity and specificity of the hematological parameters, and the role of serum B12 levels

along with knowledge of myriad clinical presentations that may help in diagnosis and initiate the treatment.

2. Materials and Methods

This is an observational clinical study undertaken in the department of neurology SSIMS & RC over a period of one year.

Patients who presented with symptoms suggestive of myelopathy or neuropathy or myeloneuropathy with low B12 levels were included for the study.

Presenting symptoms were paresthesia of lower extremities (94%, 47 patients), difficulty in getting up from squatting position (2%, 1 patient) and lhermittes sign (4%, 2 patients).

Complete hemogram and serum vitamin B12 levels were estimated for all these patients.

Patients Hb% & MCV were compared with serum B12 levels.

Patients with other causes of neuropathy, myelopathy and myeloneuropathy were excluded from the study. Serum Vitamin B12 levels were compared with hematological parameters ie Hb% and MCV.

3. Results

The study included 50 patients, 31 (62%) were females & 19(38%) were males and age ranged from 17 yrs to 79yrs.

Table 1: Duration of Symptoms

- 48 patients presented by 2weeks to 3months and 2 of them presented in < 2 weeks duration.

| Duration of Symptoms | Gender | | Total (n=50) |
|----------------------|---------------|-------------|--------------|
| | Female (n=31) | Male (n=19) | |
| 2weeks to 3months | 28(90.3%) | 19(100%) | 48(96%) |
| <2 Week | 3(9.7%) | 0(0%) | 3(6%) |

Hemoglobin percentage in these patients ranged from 8gm% to 12gm%. Patients with Hemoglobin <12gm% were considered to be anemic.

MCV ranged from 80fL to 100fL. None of the patients had normal serum Vitamin B12 levels. All the patients had decreased B12 levels i.e. < 250ng/L.

Table 2: Comparison of MCV and Hb with Vitamin B12

| Haematological abnormality | Gender | | Total (n=50) | P value |
|----------------------------|---------------|-------------|--------------|---------|
| | Female (n=31) | Male (n=19) | | |
| Hemoglobin | | | | |
| • Decreased | 19(61.3%) | 10(52.6%) | 29(58%) | 0.547 |
| • Normal | 12(38.7%) | 9(47.4%) | 21(42.0%) | |
| MCV | | | | |
| • Normal (80-100) | 12(38.7%) | 9(47.4%) | 21(42%) | 0.547 |
| • Increased(>100) | 19(61.3%) | 10(52.6%) | 29(58%) | |
| B12 | | | | |
| • <150 | 11(35.5%) | 6(31.6%) | 17(34%) | 0.565 |
| • 150-200 | 18(58.1%) | 10(52.6%) | 28(56%) | |
| • >200 | 2(6.5%) | 3(15.8%) | 5(10%) | |

21 patients had normal Hb and another 21 had normal MCV but all of them had decreased B12 levels.

4. Discussion

Vit B12 deficiency can manifest as dysaesthesia, disturbance of position sense, and spastic paraparesis or tetraparesis. Neuropathological findings in vitamin bB12 deficiency are diffuse, with multifocal pattern of axonal loss and demyelination. Most severe in the cervical and thoracic spinal cord. Initial part of the disease affects posterior columns followed by anterolateral and anterior tract involvement in the later part of the diseases.^[7]

Adenosylcobalamin is required as a cofactor for the conversion of methylmalonyl CoA to succinyl CoA. Lack of adenosylcobalamin leads to accumulation of methylmalonyl CoA, causing a decrease in normal myelin synthesis and leading to incorporation of abnormal fatty acids into neuronal lipids. Alternatively, impaired DNA synthesis could hinder oligodendrocyte growth and thus myelin production.^[8]

Even though the human body has enough vitamin B12 stores to last for up to five years, its deficiency is not uncommon. The main systems affected due to B12def are the hematological, skin and mucous membranes, and the nervous system. Neurological features are attributable to pathology in the peripheral nerves, optic nerves, posterior and lateral columns of the spinal cord and brain. B12def is a classic neurological 'system specific degeneration' in which

particular sets of neurons are affected because of their selective vulnerability

Most commonly Vitamin B12 deficiency myelopathy or neuropathy or myeloneuropathy, reportedly, are known to present in subacute to chronic duration. Little is known regarding the acute presentation of this potentially reversible disease. It's important to know for day to day practice regarding the screening of the patients with Serum B12 levels as the Hb and MCV do not always have an anemic and macrocytic or dimorphic picture. Necessitating the practicing physicians to subject patients for serum B12 assay when there is a high index of suspicion in such patients.

Similar to our study which shows a poor correlation with the Hb and MCV was shown in the study done by leishar et al^[8]. In a study done by S. Aaron, S. Kumar, J. Vijayan, J. Jacob, M. Alexander, C. Gnanamuthu^[9] correlates with our study as their study also had predominance of myeloneuropathy as majority of the patients and their study also supports the fact that presentation can be Acute in vit b12 deficiency, and also a normal Hb and MCV doesn't exclude a b12 deficiency.

One younger female 23 yr had presented with frequent falls without loss of consciousness, another 18 yr female presented with GBS like picture of areflexia and proximal weakness in the form of difficulty in getting up from squatting position without any aid which on mri revealed posterior cord T2 hyperintensity with demyelinating like features on Nerve conduction studies.

Our study emphasizes that there was no clinic hematological correlation in form that even though patient were clinically symptomatic and had normal Hb and MCV still had low b12 levels. Hence forth determining the importance of investigating for B12 levels to initiate appropriate therapy at right point of time to prevent progression to an irreversible stage.

5. Conclusions

The study emphasizes that there is no clinic hematological correlation in vitamin B12 deficiency patients who present with neurological problems.

Estimation of Vitamin B 12 levels in all the patients is mandatory for proper diagnosis and treatment to avoid irreversible sequelae of such eminently treatable deficiency disorder.

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