

## Evaluation of vitamin B12 deficiency in various clinical conditions

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**Abstract:** Low levels of vitamin B12 have been associated with several clinical conditions. However no single symptom or group of symptoms can be made responsible. Reported causes of deficiency among older population are hematologic or neurological, followed by gastrointestinal and possibly vascular symptoms. The present prospective observational study was, hence, initiated to evaluate the underlying clinical condition or symptoms associated with vitamin B12 deficiency. The study was prospective observational and carried out on 121 patients (males, n=63 and females, n=58) for the period from January 1, 2004 to January 24, 2007. Age ranges were between 16 - 70 years, and categorized as > 60 yrs and < 60 years. All blood parameters were analyzed by standardized methods on automated analyzers. The deficiency was found to be more prevalent in males and increased from 52.06% to 58.10% in individuals with vitamin B12 <150 pg/ml. Malnourishment was noted among the most subjects and weakness and anemia were frequent clinical findings (35.55%, n=43, 14%, n=51). Other clinical conditions were neuropsychiatric. Whereas less frequent findings were paraesthesia and gastrointestinal symptoms. Hypertension was more prevalent in vitamin B12 deficient individuals followed by diabetes, dementia, stroke, ischemic heart disease and Parkinson's disease.

**Key words:** Vitamin B12, neuropsychiatric, hematologic, clinical conditions

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### INTRODUCTION

Deficiency of Vitamin B12 is a common condition which is proliferated among general population. Moreover, its deficiency is common with increasing age<sup>1</sup>. Inadequate levels of vitamin B12 have been associated with group of clinical status and no single symptom, or cluster of symptoms, has been known to be associated with it. However, gastrointestinal and possibly vascular symptoms are also common<sup>1-3</sup>. The cause of deficiency among older population is reported to be hematologic or neurologic in nature, if it is untreated, complications may develop. In this regard, recent concerns have also been raised about potential adverse effects on infant growth and development in exclusively breastfed babies of mothers who adhere to a strict vegan diet<sup>1,4,5</sup>. Some commonly reported clinical conditions associated with vitamin B 12 deficiencies are hematological<sup>6,7</sup>, paresthesias<sup>6,8</sup>, glossitis, anorexia<sup>7,9</sup>, vascular manifestation<sup>10</sup>, adverse affect on infant growth and development<sup>1,11-14</sup>. The present prospective observational study was, hence, initiated to evaluate the underlying clinical condition or symptoms associated with vitamin B12 deficiency.

### MATERIALS AND METHODS

The study was carried out on 121 patients from January 1, 2004 to January 21, 2007. The patients from both indoor and OPDs were included and classified according to gender, age groups and vitamin B12 levels. Age ranges were between 16-70

years, and categorized as >60 years and <60 years. Males, n=63 and females, n=58 were included in the study. Serum folate, vitamin B12 and hemoglobin measurements performed on selected subjects were referred by physicians and practitioners for routine diagnostic check-ups to our laboratory over four years. Previously described protocols<sup>1</sup> were followed for processing and grouping of results. Blood samples from patients were routinely collected after an overnight fast. Haematological testing for Hemoglobin and MCV was performed on Sysmex analyzer. Serum folate and vitamin B12 were assayed on Elecsys 1010 and 2010 auto-immunoassay system (Roche Diagnostic, Basel), whereas creatinine and LDH were performed on Hitachi 912 chemistry analyzer (Roche Diagnostics). The CV of the B12 immunoassay is 3.7% CV and within precision 3.0%, for folate 5.0% CV and within precision 3.0%. Throughout the study the quality of results was validated by regular internal quality control procedures. Anaemia was defined as a haemoglobin concentration <14.0 g/dL in men and <12.3 g/dL in women, respectively. Low serum levels of folic acid and vitamin B12 were established at < 2.7 (normal 2.7-16.1 ng/mL) and <220 (220-925 pg/mL), respectively. The association between age and other variables was tested by multiple linear regression analysis. Data was analyzed by grouping on the basis of age, gender and vitamin B12 levels. Statistical analyses were performed using the statistical package SPSS-version 13 (USA) and results are presented as the percentage.

**RESULTS**

We conducted a prospective observational study of 121 patients with low vitamin B12 levels (<200pg/ml) from 1st Jan 2004 till 21st Jan 2007. Age limits were 15-70 years of age, where 47.93% were in age limits < 60 yrs and 52.06% in > 60 yrs (Figures 1 & 2). 58 males (47.92%) and 63 females (52.06%) were included in the study. Related lab tests done were Hb, MCV, Creatinine, vitamin B12, Folic acid, LDH. Data was analyzed by grouping on the basis of age, gender and vitamin B12 level. The study showed mean B12 level in vitamin B12 deficient individuals as 122.10±21 pg/ml. Mean concentrations of other parameters are MCV=96 fl (normal range 76-96fl), creatinine=1.3 mg/dl (0.5-1.5 mg/dl), folic acid 5.6 ng/ml (2.72-16.1 ng/ml), LDH=382 U/L (<480 U/L), bilirubin = 0.53 mg/dl (<1.0 mg/dl). About 61.15% (n=74) patients had B12 levels of < 150pg/ml comprising of elderly age (>60yrs). Deficiency was found to be more prevalent in males and increased from 52.06% to 58.10% in individuals with vitamin B12 <150 pg/ml (Figure 4). Most patients were noted to be malnourished. Weakness and anemia were more frequent clinical findings (35.55%, n=43;14%, n=51) (Figure 5). Other clinical conditions were neuropsychiatric symptoms (13.22%-15.70%) such as urinary or fecal incontinence, drowsiness, polyneuritis, ataxia and impaired memory. Less frequent findings were paraesthesia and gastrointestinal symptoms (6.5%-9.0%). Mean Hb was low, mean folic acid, LDH and bilirubin levels were normal (Figure 6). Hypertension was more prevalent in vitamin B12 deficient individuals followed by diabetes, dementia, stroke, ischemic heart disease and Parkinson's disease (Figure 7).

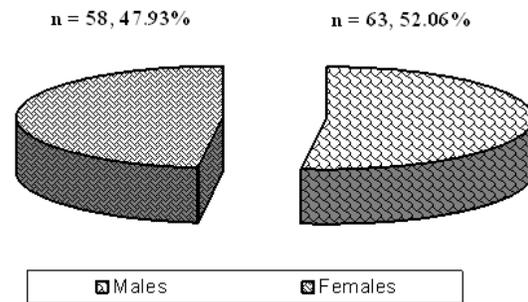
**DISCUSSION**

It is reported that no single symptom or cluster of symptoms have been linked to deficiency of vitamin B12<sup>1</sup>. However it is evident that B12 deficiency usually appears nearly at about 60 years of age as it remain asymptomatic for many years<sup>1, 15</sup>. We have found that deficiency is prevalent in elderly males and percentage of affected males increased when the same was assessed in group with vitamin B 12 less than 150pg/ml. Different general clinical manifestations, that were noted during our study in B12 deficient individuals, were anemia (42.14%), generalized weakness (35.5%), drowsiness (15.7%), urinary or fecal incontinence

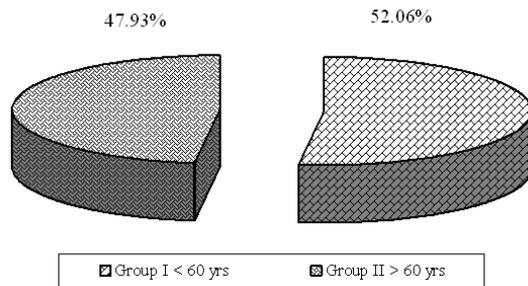
(19%), followed by polyneuritis (13.2%) and ataxia (13.22%).

**Table 1:** Hematological and Biochemical parameters in vitamin B12 deficient patients.

Parameters	Concentrations	Normal ranges
Hb Males	10.46 ± 2.1	13-18 gm/dl
Females	8.93 ± 1.8	11.5-16.4 gm/dl
MCV	96 ± 2.3	76-96 fl
Creatinine	1.3 ± 0.34	0.5-1.5 mg/dl
LDH	382 ± 12.6	< 480 U/L
Vitamin B12 Group I <150	122.10 ± 21.0	220-925 pg/ml
Group II 150-220	152.26 ± 19.5	220-925 pg/ml
Folate	5.6 ± 1.1	< 1.0 mg/dl



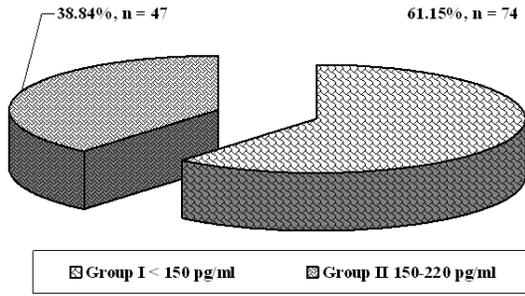
**Figure 1:** Gender wise distribution of vitamin B12 deficient patients.



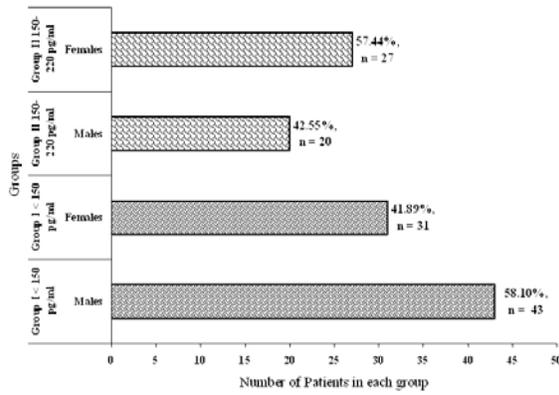
**Figure 2:** Age wise distribution of vitamin B12 deficient patients.

Groups of vitamin B12 deficient individuals have been reported with several clinical conditions and disease to be associated with vitamin B12 deficiency both in adults and elderly population<sup>6-14</sup>. In this regard, hematological disorder is worthy to mention, however, this situation is rare in the United States, but are often severe and irreversible in the children, the majority of which, with clinical deficiency, will have signs of megaloblastic anemia.

In various studies 56% to 77% of patients had signs of macrocytosis or anemia<sup>8,16-19</sup>, with overt vitamin B12 deficiency.



**Figure 3:** Distribution of vitamin B12 deficient patients according to vitamin B12 status.



**Figure 4:** Gender wise distribution in vitamin B12 deficient patients.

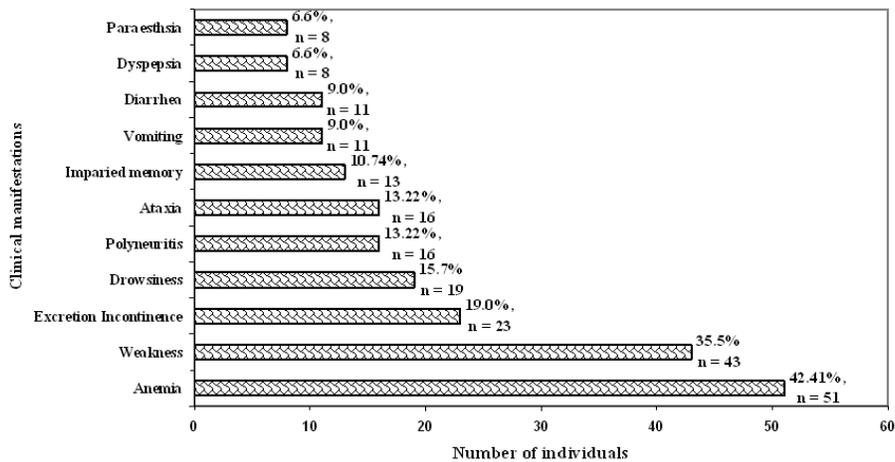
Common neurologic manifestation, that may follow vitamin B12 deficiency or vice versa includes paresthesias (with or without objective

signs of neuropathy), weakness, motor disturbances (including gait abnormalities), vision loss, and a wide range of cognitive and behavioral changes (e.g., dementia, hallucinations, psychosis, paranoia, depression, violent behavior, and personality changes)<sup>1</sup>. Tingling of the hands and feet is perhaps the most common neurologic complaint<sup>1,6,8,20</sup>. In general, patients may develop neuropsychiatric manifestations such as combined sclerosis of spinal cord (classic finding), polyneuritis, ataxia and babinski's phenomenon (frequent finding) and cerebral syndromes, urinary and fecal incontinence (rare)<sup>1</sup>.

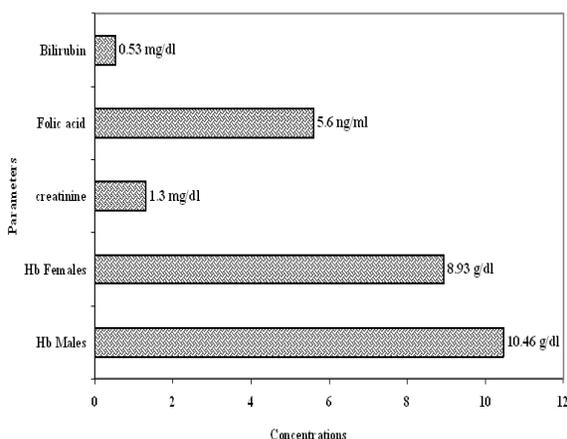
It is also documented that gastro-intestinal manifestations may also precede Vitamin B12 deficiency<sup>1,7,9</sup>. Frequently noted symptoms include anorexia, flatulence, diarrhea, and constipation<sup>7,9,21,22</sup>. It is observed that these symptoms can develop among patients with a vitamin B12 deficiency even without associated anemia, macrocytosis, or overt neurologic defects<sup>1</sup>.

Another very important condition that might prevail both low vitamin B12 levels and low folate levels, is the development of vascular complications due to elevated levels of homocysteine (Hcy)<sup>1,10,23</sup>. Hyperhomocysteinemia thus increases the risk of developing a vascular occlusion<sup>10,23</sup>, therefore potentially enhancing the risk of coronary heart disease and ischemic stroke<sup>23-25</sup>.

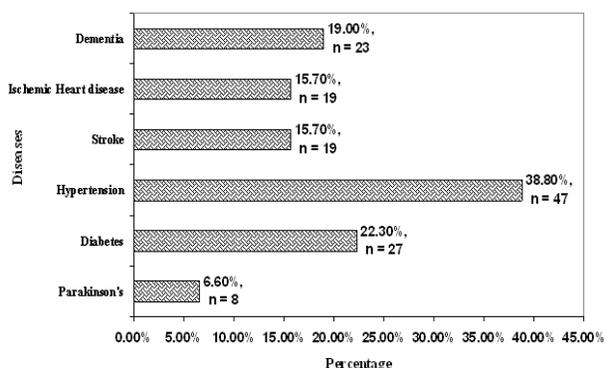
Furthermore, it is also well documented that nursing infants of mothers who adhere to a strict vegetarian or vegan diet throughout their pregnancy and while breastfeeding might also experience serious vitamin B12-related deficiency effects<sup>11,12,14,22</sup>.



**Figure 5:** Clinical manifestations in vitamin B12 deficient patients.



**Figure 6:** Biochemical and hematological parameters in vitamin B12 deficient patients.



**Figure 6:** Occurrence of different diseases in vitamin B12 deficient patients.

Additionally, several cases of significant vitamin B12 deficiencies among infants and young children have been reported<sup>11-14</sup> which may proceed to induce clinical manifestations which are typical of older patients, such as hematologic, neurologic, gastrointestinal, and cardiovascular consequences<sup>11-14,26,27</sup>. Furthermore, low or marginal vitamin B12 status in pregnant women increases the risk for neural tube birth defects<sup>28</sup>.

### CONCLUSION

In conclusion, the present study evaluates various clinical conditions in patients deficient in vitamin B12. It was observed that males are more affected and the affect is more adverse in those with vitamin B 12 levels of <150 pg/ml. Weakness and anemia were more frequent clinical findings, in addition to other clinical conditions such as neuropsychiatric symptoms (urinary or fecal incontinence, drowsiness, polyneuritis, ataxia and

impaired memory). Less frequent findings were paraesthesia and gastrointestinal symptoms.

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