

## Clinicopathological Correlation of Pancytopenia

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### Abstract

*Objectives:* Increasing number of patients present now a days with pancytopenia due to B12 and folic acid deficiencies, bone marrow failures and hypersplenism. The changing diet, lifestyle, and environment could be the cause for the increased incidence. It is important to have a clinical diagnosis at presentation itself, to identify and treat the potentially correctable causes of pancytopenia like vitamin B12 deficiency. The present study was to look into the correlation between clinical diagnosis and final diagnosis; and also to study the clinical profile, etiological factors, and treatment response in the subgroup of patients diagnosed to have B12/folate deficiency. *Methods:* It was a cross-sectional study involving 65 patients in one year. Their clinical diagnosis (made after history, physical examination and hemogram) was compared with the final diagnosis. The subgroup of patients diagnosed to have B12/folate deficiency was studied in detail for their clinical profile & etiological factors. *Results:* There was a statistically significant correlation between clinical & final diagnosis. Sensitivity of clinical diagnosis was highest (93%) for B12/folate deficiency. Diet history, knuckle pigmentation, glossitis and MCV>100fl had a statistically significant association with B12/folate deficiency. *Conclusions:* B12/folate deficiency and acute leukemia were the commonest causes for pancytopenia. Sensitivity of clinical and pathological diagnoses of B12 deficiency was 93% and 73% respectively. Hence high clinical suspicion is mandatory for diagnosis of vitamin B12 deficiency. The diagnosis of vitamin B12/folate deficiency can be predicted using the dietary history, knuckle pigmentation, glossitis and MCV>100fl.

**Keywords:** Pancytopenia; B12 Deficiency; Folic Acid Deficiency; Clinico-Pathological Correlation.

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### Background & Objectives

Pancytopenia is an important clinico-haematological entity encountered in our day to day clinical practice, characterized by simultaneous decrease in number of white blood cells, red blood cells and platelets. The spectrum of disorders primarily or secondarily affecting the bone marrow may manifest with peripheral pancytopenia. Underlying pathology determines the management and prognosis of the patients. Pancytopenia as a clinical problem is becoming more common now a days with increasing number of B12 and folic acid

deficiencies and the increasing number of bone marrow failures by several mechanisms and pancytopenia due to hypersplenism. The changing diet, lifestyle and environment cause an increase in incidence of pancytopenia in recent years. It is important to have a clinical diagnosis at presentation itself, to identify and treat the potentially correctable causes of pancytopenia like vitamin B12 deficiency. The present study was carried out to look into the correlation between clinical diagnosis and final diagnosis; and also to study the clinical profile, etiological factors and treatment response in the subgroup of patients diagnosed to have B12/folate deficiency.

**Methods**

The present study was a cross-sectional study conducted at Department of General Medicine and Hematology, Govt. Medical College, Kozhikode. 65 patients participated in the study; their clinical diagnosis (made after history, physical examination and hemogram) was compared with the final diagnosis (made after clinical evaluation, appropriate investigations and a period of follow up). The subgroup of patients diagnosed to have B12/folate deficiency was studied in detail about their clinical profile, etiological factors and treatment response. Duration of study was one year; data was analyzed in SPSS software.

**Results**

Total of 65 patients presented with pancytopenia during the study period. B12/folate deficiency and

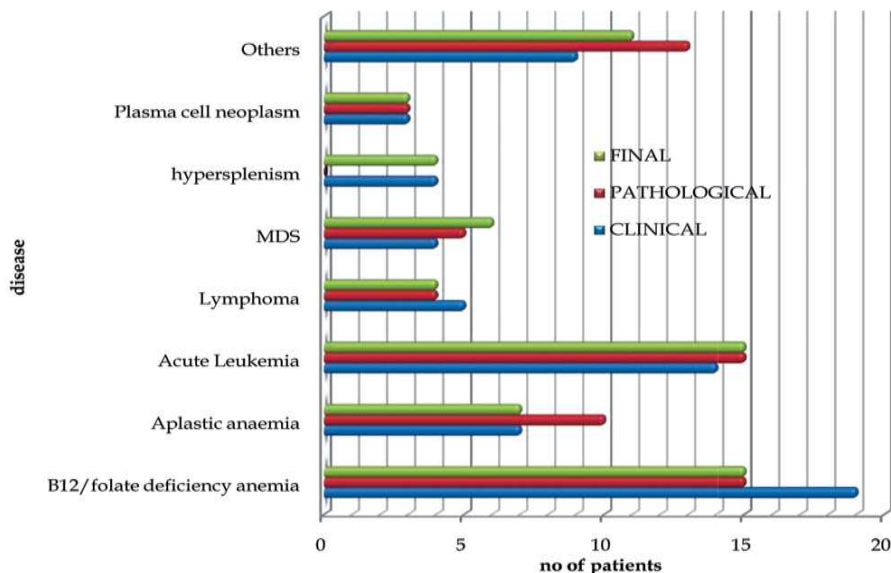
acute leukemia constituted maximum number of cases, i.e. 15 patients each (23%).

Sensitivity of clinical diagnosis in the present study was highest for vitamin B12/folate deficiency (93%) and that of acute leukemia is 80%. Histopathology could suggest a diagnosis of vitamin B12/folate deficiency only in 73% cases. The kappa agreement in the present study is 0.76(76%) with a p-value <0.001. That means, the correlation between the clinical diagnosis and final diagnosis in the study is statistically highly significant.

B12/folate deficiency was found maximum in the middle aged people, that too with a slight female preponderance. B12 deficiency was found more among house-wives and manual labourers. Most common symptom was fatigability, and the commonest sign was knuckle pigmentation. There was a statistically significant association between vegetarian diet or dietary inadequacy with vitamin B12 deficiency. Also there was a highly significant association for knuckle pigmentation, pedal edema,

**Table 1:** Comparison between clinical, pathological and final diagnoses

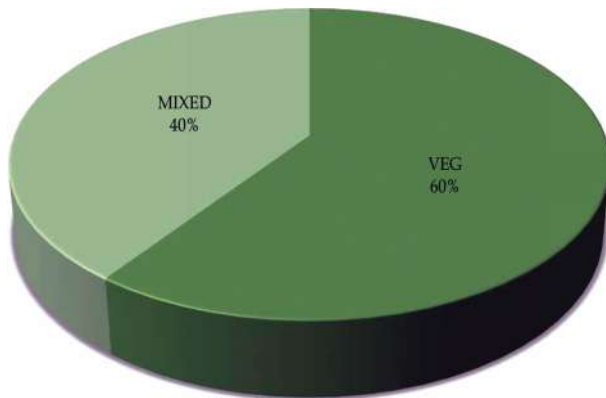
Disease	Clinical		Diagnosis Pathological		Final	
	Frequency	%	Frequency	%	Frequency	%
B12/Folate Deficiency Anemia	19	29	15	23	15	23
Aplastic anaemia	7	10.8	10	15.4	7	10.8
ACUTE LEUKEMIA	14	21.5	15	23	15	23
Lymphoma	5	7.7	4	6.2	4	6.2
MDS	4	6.2	5	7.7	6	9.2
hypersplenism	4	6.2	0	0	4	6.2
Plasma cell neoplasm	3	4.6	3	4.6	3	4.6
Others	9	13.8	13	20	11	16.9



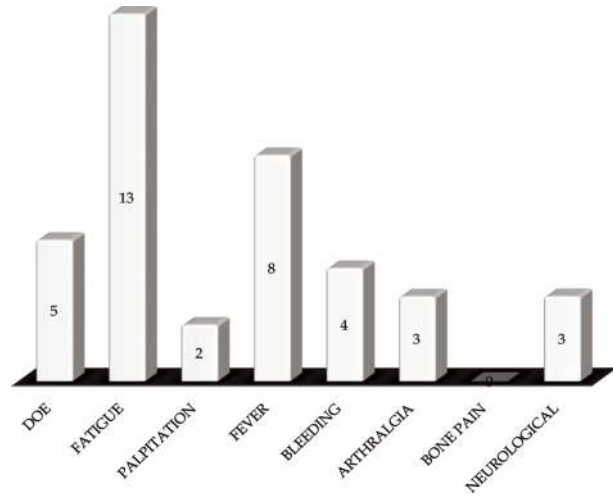
**Graph 1:** Comparison between clinical, pathological and final diagnoses

**Table 2:** Physical signs observed in patients with B12 deficiency

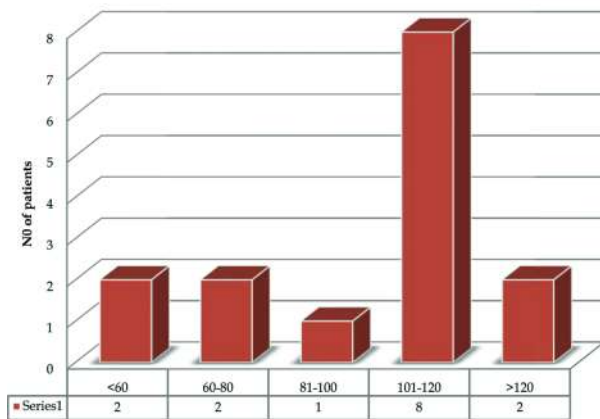
Signs	Frequency	Percent	Total	P-Value
Pallor	15	100	15	*
Icterus	1	7	15	0.696
Lymphadenopathy	1	7	15	0.865
<i>Pedal Edema</i>	8	53	15	<b>0.047</b>
<b>Knuckle Pigmentation</b>	<b>10</b>	<b>67</b>	<b>15</b>	<b>0.0001</b>
Bleeding Spots	4	27	15	0.582
<i>Glossitis</i>	6	40	15	<b>0.014</b>
Hepatomegaly	4	27	15	0.664
Splenomegaly	2	13	15	0.169



**Graph 2:** Diet pattern in B12 deficiency



**Graph 3:** Symptomatology in B12 deficiency



**Graph 4:** Distribution of MCV in B12 deficiency

glossitis & MCV>100fl with B12/folate deficiency anemia. Total leucocyte count <1000/cmm or platelet count <20,000/cmm were found to be unusual in B12 deficiency. Macrocytic picture in peripheral smear and Erythroid hyperplasia with megaloblastic change in bone marrow also suggested diagnosis of B12 deficiency in the present study. Also there was a statistically significant positive correlation between age & MCV in patients with B12/folate deficiency. B12 assay was not found to be a reliable diagnostic test.

**Conclusions**

1. When pancytopenia is the major clinical problem, megaloblastic anemia and acute leukemia are the most common diseases to be considered in our set up.
2. Clinical diagnosis of megaloblastic anemia is possible with a sensitivity of 93% & specificity of 90%, while that of acute leukemia is possible with a sensitivity of 80%.
3. It is very important to arrive at the clinical diagnosis for the etiology of pancytopenia before proceeding with invasive investigations.
4. In B12/folate deficiency, one has to depend more on clinical diagnosis because sensitivity of clinical diagnosis was 93% while that of pathological diagnosis was only 73%.
5. B12 deficiency is more common in middle aged people, more in housewives and manual laborers.
6. B12 deficiency was more common among strict vegetarians or those whose diet is grossly inadequate.

7. Knuckle pigmentation is one of the most diagnostic physical sign in B12 deficiency.
8. Very low total leucocyte count (<1000/mcl) and platelet count (<20,000/mcl) are rare in B12/folate deficiency.
9. Mean corpuscular volume >120fl, macrocytic picture in peripheral smear and erythroid hyperplasia with megaloblastic change in bone marrow studies support the diagnosis of B12/folate deficiency.
10. The diagnosis of vitamin B12/folate deficiency can be predicted using the variables DIET, Knuckle Pigmentation, and MCV>100fl which was statistically significant.
11. B12 assay is not a reliable method for diagnosis or assessing treatment response.
12. Good clinical evaluation is the backbone of accurate diagnosis even today.

#### Acknowledgments

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