

TO STUDY THE CLINICAL SPECTRUM AND HAEMATOLOGICAL ABNORMALITIES IN PATIENTS OF MACROCYTIC ANAEMIADaljinderjit Kaur¹, Gurinder Mohan², Narottam Bhalla³**HOW TO CITE THIS ARTICLE:**

Daljinderjit Kaur, Gurinder Mohan, Narottam Bhalla. "To Study the Clinical Spectrum and Haematological Abnormalities in Patients of Macrocytic Anaemia". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 51, June 25; Page: 8900-8904, DOI: 10.14260/jemds/2015/1288

ABSTRACT: BACKGROUND: Folate and vitamin12 deficiency have been known to cause megaloblastic anaemia. Megaloblastic anaemia is not uncommon in India, but data are insufficient regarding its prevalence, causative factors and precipitating factors. **AIMS & OBJECTIVES:** To evaluate the clinico-haematological profile in patients of macrocytic anaemia. **MATERIAL AND METHODS:** In the present study, 50 patients of >20years of age with hemoglobin <10g/dl, Mean corpuscular volume > 95 fl and PBF showing macrocytosis and pancytopenia were included. Detailed history with clinical examination was performed and investigations (Bone Marrow aspiration, Serum Folate and cobalamin assays) were carried out. **RESULTS:** The peak incidence of megaloblastic anaemia was in the age group of 41-50 years (48%), with male preponderance (71%). (The predominant symptoms were fatigue (54%) followed by low grade fever (52%), breathlessness (50%), and mild jaundice (22%.) (Physical findings were pallor (88%), hepatomegaly (80%), knuckle hyperpigmentation (68%), glossitis (50%), peripheral neuropathy (28%) and mild icterus was the least common finding in 22% of patients. 64% patients of macrocytic anaemia were found to be lactovegetarian. Cobalamin deficiency was present in maximum patients (50%), followed by combined cobalamin and folate deficiency in 34% and folate deficiency in 16% of patients. Bonemarrow smears revealed megaloblastic picture in 58% of patients and 42% patients had non-megaloblastic bone marrow picture. **CONCLUSION:** Megaloblastic anaemia must be considered in the differential diagnosis of patients presenting with pyrexia of unknown origin, mild icterus or pancytopenia. Therefore, the early screening for cobalamin and folic acid deficiency can lead to improvement in the wellbeing and prolongs the life of people in our community.

KEYWORDS: RBC, DNA, MCV, MCH, MCHC.

INTRODUCTION: Nutritional anaemias until recently have been relatively neglected and frequently they remain undiagnosed.^[1] One of the reasons could be that symptoms and signs are much less obvious and develops over a protracted course of time. Macrocytic anaemia describes as an anaemic state characterized by the presence of abnormally large RBC's in the peripheral blood. Macrocytic anaemia can usually be divided into two categories: Megaloblastic and non Megaloblastic anaemia, based on the examination of the bone marrow. This categorization is important and frequently aids in determining the etiology of the anaemia.^[2]

Megaloblastic anaemias are disorders resulting from abnormal maturation of haematopoietic stem cells due to inhibition of DNA synthesis, and two vitamins namely, Cobalamin (Vitamin B12) and Folic acid are essential for DNA biosynthesis. Deficiency of either vitamin results in asynchrony in the maturation of the nucleus and cytoplasm of rapidly regenerating cells.^[3] Nonmegaloblastic macrocytic anemias are those in which no impairment of DNA synthesis occurs. Included in this category are disorders associated with increased membrane surface area, accelerated erythropoiesis, alcoholism, and chronic obstructive pulmonary disease (COPD).^[4]

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AIMS AND OBJECTIVES:

1. To study the clinical spectrum in patients of macrocytic anaemia.
2. To evaluate the etiology and hematological abnormalities in patients of macrocytic anaemia.

MATERIAL AND METHODS: A hospital based retrospective analysis of all patients presented and diagnosed as Megaloblastic anaemia was done .The study included 50 patients of age >20years, of either sex, who were found to be having macrocytic anaemia with hemoglobin level <10g/dl, Mean corpuscular volume(MCV) > 95 fl and Peripheral blood film findings showing macrocytosis and pancytopenia. Patients with dimorphic anaemia were excluded from the study.

The data collected was analysed and a multivariate analysis was done to determine correlation between symptoms, signs and hematological investigations including Bone Marrow aspiration, serum folate and cobalamin assays and Upper GI Endoscopy. Chi-square analysis was used to compare percent patients with vitamin deficiency with percent patients with vitamin-normal status.

RESULTS: A descriptive study was conducted with the aim to study the clinical spectrum and hematological abnormalities in patients of Macrocytic anaemia. In the present study, patients presented in the department of medicine at SGRDIMSR, Amritsar; with features of macrocytic anaemia were taken for study. A detailed clinical history with emphasis on predisposing factors, associated clinical conditions, physical examination and complete hematological examination along with Bone marrow aspiration and Vitamin B12, folate assays were carried out.

Megaloblastic anaemia was more common in males, which outnumbered the females by the ratio of 1.7:1. Overall the maximum patients with macrocytic anaemia were in the 41-50 year age group (26%) and minimum patients (10%) were in the age group >60 years. The mean age of presentation was 45years in males and 37years in females. Fatigue was the most common symptom (54%) followed by low grade fever (52%), breathlessness in 50% and yellowish discolouration of eyes was present in only 22% of patients. On clinical examination, pallor was the most common finding in 88%, followed closely by hepatomegaly (80%), knuckle hyperpigmentation (68%), glossitis (50%), peripheral neuropathy (28%) and mild icterus was the least common finding in 22% of patients.

Mean hematological parameters included hemoglobin as 5.70±1.7 gm/dl, MCV-107.08±8.7fl, MCH-34.03±3.9pg, MCHC-32.24±2.1g/dl, Platelet count-1.66±0.712 and Reticulocyte count-0.954±0.839. Pure cobalamin deficiency was seen in majority of patients (44%) as a cause of Megaloblastic anaemia, followed by combined cobalamin and folate deficiency in 40%patients and pure folate deficiency in 16% patients. The bone marrow examination revealed megaloblastic picture in 58% of patients and 42% patients had non-megaloblastic bone marrow picture.

PARAMETERS	MEAN VALUE
Hemoglobin	5.70±1.7
Mean Corpuscular Volume	107.08±8.7
Mean Corpuscular Hemoglobin	34.03±3.9
Mean Corpuscular Hemoglobin Concentration	32.24±2.1

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Total Leucocyte Count	8024.40±4520.97
Platelet Count	1.666±0.712
Reticulocyte Count	0.954±0.839

Table 1: Showing mean value of hematological parameters taken in the present study

Mean values of haemoglobin, MCV, serum vitamin B12 and serum folate were not significantly different between males and females and were found to be statistically non-significant.

Variable	MALE (n = 32)	FEMALE (n = 18)	p-value
Age(years)	45.34±14.18	37.17±11.79	0.043*
Hemoglobin(g/dl)	5.64±1.56	5.81±1.99	0.735 ^{NS}
MCV(fl)	106.19±7.49	108.67±10.75	0.343 ^{NS}
S.Vitamin B12(pg/ml)	202.04±105.94	239.97±121.79	0.255 ^{NS}
S.folate(ng/ml)	7.88±5.23	5.95±2.77	0.154 ^{NS}

Table 2: Demographic and clinical characteristics of patients

Variable	Correlation Coefficient	p - value
Age(years)	-0.135	0.351 ^{NS}
Hemoglobin(g/dl)	-0.259	0.069 ^{NS}
S. Vitamin B12(pg/ml)	-0.126	0.382 ^{NS}
S.Folate (ng/ml)	0.210	0.144 ^{NS}

Table 3: Correlation of age, hemoglobin, Vitamin B12 and folate with MCV

In the study, no association was found between hemoglobin, serum vitamin B12, Serum folate levels with MCV levels, as determined by Spearman's correlation test.

The most common etiology for macrocytic anaemia was Alcoholism in 24%, dietary deficiency in 18%, drug induced and ileocaecal tuberculosis in 12%, followed closely by ileitis, inflammatory bowel disease, atrophic gastritis, intestinal amoebiasis, celiac disease and least common in jejunal diverticula, hypothyroidism and H.Pylori.

DISCUSSION: Macrocytic anaemia is one of the preventable and treatable causes of nutritional anaemia. Macrocytic anaemia is either due to Vitamin B12 deficiency or folate deficiency or both. Folic acid and Vitamin B12 are essential dietary components for humans, because they are required for DNA synthesis. Haematopoietic cells (having a very high turnover) are especially sensitive to deficiencies of folate and vitamin B12. With derangement of DNA synthesis due to deficiencies of these vitamins, Megaloblastic anaemia ensues.^[5]

Recent insights into the clinical, haematological, bio-chemical, endoscopic studies have shown varied clinical spectrum of Megaloblastic anaemia. These may vary from symptoms of anaemia to various neuropsychiatric manifestations and gastrointestinal manifestations.

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Based on the western literature there is a perception that folate deficiency is the main cause of Megaloblastic anaemia. Cobalamin deficiency was responsible for Megaloblastic anaemia in the majority of our patients (44%), followed by 40% with combined deficiency and pure folate deficiency accounted for 16%.

The majority of our patients were lactovegetarians, i.e., found in 64% patients of macrocytic anaemia. The average Indian vegetarian diet is deficient in cobalamin.^[6] An earlier pilot study reported by us had shown that 40% of normal Indian subjects with normal haemograms were cobalamin-deficient.^[7] A 1973 study by WHO on the nutritional status of pregnant women in India documented iron, folate and cobalamin deficiency.^[8]

We attempted to identify factors that might be responsible for converting occult cobalamin deficiency into florid Megaloblastic anaemia. In Caucasian and Chinese populations, Megaloblastic anaemia is reported to occur in older age groups with an equal sex ratio or male preponderance.^[9,10] In contrast, the peak incidence in our study was seen in the age group of 41-50 years (18% of patients) and there was a preponderance of males (64%).

For a laboratory diagnosis of Megaloblastic anaemia, a CBC with red cell indices, examination of a well stained blood film and assay of the 2 vitamins are sufficient to make a definitive diagnosis. Macrocytosis was most common finding on peripheral blood film in 42% patients, pancytopenia in 28% where as 8% patients showed anisocytosis and nucleated RBCs each. Other authors have also observed that Megaloblastic anaemia must be an important differential diagnosis in patients presenting with pancytopenia.^[11,12] Bone marrow examination does not contribute to the diagnosis of the underlying aetiology and should be done when a diagnosis of myelodysplasia is being considered.

SUMMARY AND CONCLUSIONS: In conclusion, Megaloblastic anaemia causes substantial morbidity in patients with anaemia. Data regarding the magnitude of the problem in different parts of India and the factors that might influence its incidence are lacking. Megaloblastic anaemia must be considered in the differential diagnosis of patients presenting with pyrexia of unknown origin, mild icterus or pancytopenia. Documentation of occult cobalamin deficiency in different ethnic and socioeconomic groups and in pregnant women needs to be done.

Although the number of patients undergoing investigation were less, yet the improvement in the quality of life of patients undergoing treatment after ascertaining the type of anaemia and etiology of macrocytic anaemia helped us to establish further management of the patients. The early screening for cobalamin and folic acid deficiency of patients with minor symptoms of anaemia can lead to improvement in the wellbeing and prolongs the life of people in our community.

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AUTHORS:

1. Daljinderjit Kaur
2. Gurinder Mohan
3. Narottam Bhalla

PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Internal Medicine, PGIMER, Chandigarh.
2. Professor & HOD, Department of Internal Medicine, SGRDIMS & R, Sri Amritsar.

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3. Professor, Department of Internal Medicine, SGRDIM & R, Sri Amritsar.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Daljinderjit Kaur,
House No. 57, Sector 15-A,
Chandigarh.
E-mail: dkaur2210@gmail.com

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