



A STUDY OF CLINICAL PROFILE OF MEGALOBlastic ANEMIA AN OBSERVATIONAL STUDY

General Medicine

Manish Sharma

Associate Professor, Department of Medicine, Gajra Raja Medical College, Gwalior, M.P., India

Naveen Saini

Junior Resident, Department of Medicine, Gajra Raja Medical College, Gwalior, M.P.

ABSTRACT

Background: Megaloblastic anaemia has been recognized as a clinical entity for over a century. Thomas Addison provided the first clinical description of pernicious anaemia, one of the known causes of megaloblastic anaemia, in 1849. This type of anaemia results from abnormal maturation of hematopoietic cells due to defective DNA synthesis. **Objectives:** To study clinical profile of Megaloblastic anaemia. **Patients and Methods:** Team of trained residents under the guidance of senior consultant, the study was hospital based observational study which include indoor and outdoor patients diagnosed with Megaloblastic anaemia based on a combination of history, clinical findings, CBC, peripheral smear. **Conclusion:** Females in the age group of 21 to 30 years were more commonly affected by Megaloblastic anaemia, Vegetarian diet can be one of the contributing factors for Megaloblastic anaemia, as majority of Megaloblastic anaemia patients were vegetarian in this study. Fatigability and pallor are the most common symptom and sign of Megaloblastic anaemia.

KEYWORDS

Peripheral Smear, Pernicious Anaemia.

INTRODUCTION

Megaloblastic anaemia has been recognized as a clinical entity for over a century. Thomas Addison provided the first clinical description of pernicious anaemia, one of the known causes of megaloblastic anaemia, in 1849.[1] This type of anaemia results from abnormal maturation of hematopoietic cells due to defective DNA synthesis. Two essential vitamins, cobalamin (vitamin B12) and folic acid, are crucial for DNA biosynthesis. Deficiency in either vitamin leads to asynchronous maturation of the nucleus and cytoplasm in rapidly regenerating cells. In the hematopoietic system, this asynchrony causes abnormal nuclear maturation alongside normal cytoplasmic maturation, leading to apoptosis, ineffective erythropoiesis, intramedullary haemolysis, pancytopenia, and distinctive morphological abnormalities in blood and marrow cells.[2] This ineffective erythropoiesis is accompanied by intramedullary haemolysis, resulting in elevated levels of lactate dehydrogenase and indirect bilirubin in the serum.[3]

Megaloblastic anaemia can cause significant morbidity if not properly identified or misdiagnosed. Its causes are multifactorial and can stem from dietary deficiencies, impaired absorption and transport, or impaired utilization of vitamins crucial for DNA synthesis. In India, with its diverse ethnic populations and varying dietary and social customs, the incidence of megaloblastic anaemia and its associated complications have not been sufficiently documented.[4] It is crucial to consider megaloblastic anaemia as a key differential diagnosis in patients presenting with pancytopenia.

Hematological Findings

Peripheral blood smear In megaloblastic anaemia showing oval macrocytes with significant anisocytosis and poikilocytosis are prominent features. The mean corpuscular volume (MCV) typically exceeds 100 fL, unless there is an underlying cause of microcytosis, such as iron deficiency or thalassemia trait. Additionally, some neutrophils may exhibit hypersegmentation, characterized by more than five nuclear lobes. (Figure 1)

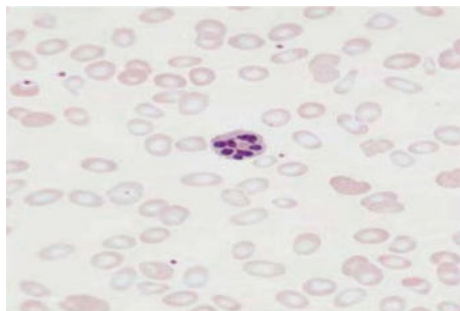


Figure 1: Peripheral Blood in severe Megaloblastic Anemia

Aims and Objectives

1. To study the clinical profile of patients with Megaloblastic anaemia.
2. To study the underlying etiological cause of the Megaloblastic anaemia.

Patients and Methods

Source Of Data: Department of General Medicine, G.R. Medical College, Gwalior (M.P.) from august 2022 - Jun 2024.

Study Type: Prospective study

Duration of Study: AUGUST 2022 to MARCH 2024

Study Design: The study were a hospital based observational study which were include indoor and outdoor patients diagnosed with Megaloblastic anaemia based on a combination of history, clinical findings, CBC, peripheral smear Sample.

Size: The study comprise minimum 130 patients

Sample size calculated by the formula:

$$n = \frac{Z^2_{\alpha/2} \times PQ}{D^2}$$

Where $Z_{\alpha/2} = 1.96$, $P = 9.1$, $Z^2_{\alpha/2} \times PQ = \dots$ $D^2 Q = 90.09$, THUS $n = 130$

Inclusion Criteria

1. Age > 15 years
2. Anaemia (Hb < 13.5 g/dl in male, 11.5 g/dl in female)

Exclusion Criteria

1. Patients who have received or are receiving cancer chemotherapy
2. Patients who have received or are receiving radiotherapy
3. Patient with age < 15 years
4. Patients who recently received blood transfusion.

Data Collection

All Patients after obtaining a detailed medical history and physical examination the following investigations will be done

1. Haemoglobin
2. Total count, differential count and ESR
3. Platelet count
4. Peripheral smear study with reticulocyte count
5. Bone marrow smear study (if indicated)

Other Investigations as Per Clinical Profile

1. Serological study for HIV infection.
2. Chest X-ray
3. USG abdomen and pelvis

Statistical Analysis

All the data were entered in a data collection sheet in an Excel format and analysed using SPSS Software. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. Probability value (p) value

less than 0.05 was considered a statistically significant.

OBSERVATIONS

This Study included total 130 patients diagnosed with Megaloblastic anemia. All the study patients were subjected to investigations including haemoglobin, total leukocyte count (TLC), platelet, peripheral smear study and bone marrow study (if indicated). Data thus collected was subjected to statistical analysis and following results were drawn.

1. Age Distribution of Study Patients:

In this study, mean age of study patients was 33.35 ± 15.99 years and median age was 30 years, with the age ranging from 15 to 89 years. Majority of patients were in the age group of 21-30 years (27.69%), followed by 31-40 years (23.07%), ≤ 20 years (20.76%), above 51 years (19.23%), and 41-50 years (9.23%) ($Z=0.4961$, $p=0.7098$).

2. Gender Distribution of Study Patients

In this study, out of 130 patients, 80 were female (61.5%) and 50 were male (38.5%). Thus, proportion of females with Megaloblastic anaemia In this study was significantly higher than males ($Z=3.721$; $p=0.0003$).

Co-morbidities in Study Patients: In this study, of 130 patients, only 16 patients (12.30%) had co-morbidities, while 114 patients (87.7%) did not, which was statistically significant ($p<0.000$).

Co-morbidities observed in study patients included chronic liver disease (CLD) in 7 patients (5.4%), chronic kidney disease (CKD) in two patients (1.5%), chronic obstructive pulmonary disease (COPD) in two patients (1.5%), hypertension (HTN) in two patients (1.5%), abdominal tuberculosis in one patient (0.76%), systemic lupus erythematosus (SLE) in one patient (0.76%), and both CLD and COPD in one patient (0.76%). (Table 1)

Table 1: Comorbidities in Study Patients

Comorbidities	Frequency	Percent (%)
Abdominal Tuberculosis	1	0.76
CKD	2	1.5
CLD	7	5.4
CLD, COPD	1	0.76
COPD	2	1.5
HTN	2	1.5
SLE	1	0.76
None	114	87.7
Total	130	100.0

Presenting Symptoms of Study patients: The most common presenting symptom in this study was fatiguability which was observed in 129 out of 130 patients (99.2%), followed by palpitation in 83 patients (63.8%), fever in 54 patients (41.5%), respiratory difficulties in 22 patients (16.9%), bleeding manifestations in only 3 patients (2.3%), and loose stools in only one patient. Thus, fatiguability was the most common presenting symptom, while bleeding manifestations and loose stools were the least common presenting symptoms of Megaloblastic anemia in this study ($p<0.0001$) (Table 2)

Table 2: Presenting Symptoms of Study Patients

Presenting Symptoms	Frequency	Percent (%)	p-value
Fatiguability	No	1	<0.0001
	Yes	129	
Fever	No	76	58.5
	Yes	54	
Palpitation	No	47	36.2
	Yes	83	
Respiratory difficulties	No	108	83.1
	Yes	22	
Bleeding manifestations	No	127	97.7
	Yes	3	
Loose stools	No	129	99.2
	Yes	1	

Clinical Findings in Study Patients: In this study, pallor was observed in all the patients (100%). Icterus was observed in 8 patients (6.15%), and pedal edema was present in 81 patients (62.30%). Other

clinical findings included koilonychia in 14 patients (10.76%), muscle wasting in 34 patients (26.15%), raised jugular venous pressure (JVP) in 5 patients (3.84%), glossitis in 4 patients (3.07%), and ESM in one patient (0.76%). Thus, the most common clinical finding in pancytopenia patients was pallor ($p<0.0001$), followed by pedal edema

Laboratory Investigations in Study Patients: Descriptive analysis showed that the mean level of haemoglobin (Hb) in this study was 6.19 ± 1.85 gm/dl, mean total leukocyte count (TLC) was 2548.32 ± 759.84 /mm³, and mean platelet count was 56206.15 ± 25725.67 /mm³. The mean level of mean corpuscular volume (MCV) was 97.08 ± 18.68 fl. The range of Hb was 1.70-10.50 gm/dl, TLC was 172–4900 /mm³, platelet count was 10000–100000 /mm³, and MCV was 58–129 fl

Bone Marrow Analysis in Study Patients: In this study, bone marrow analysis was done in 6 patients (4.60%), of which, hypercellular bone marrow was observed in 3 patients (2.30%) and hypocellular bone marrow in 3 patients (2.30%)

Severity of Anemia in Study Patients: In this study, out of 130 patients, severe anaemia was observed in 108 patients (83.1%), followed by moderate anaemia in 21 patients (16.2%), and mild anaemia was observed in only one patient (0.8%). Proportion of patients with severe anaemia was significantly higher in this study ($p<0.0001$).

Severity of Leukopenia in Study Patients: In this study, leukocyte count was normal in 46 patients (35.4%). Majority of the patients demonstrated mild leukopenia (44.6%), followed by moderate leukopenia in 24 patients (18.5%), and severe leukopenia in 2 patients (1.5%). Proportion of patients with mild leukopenia was significantly higher in this study ($p<0.0001$)

Severity of Thrombocytopenia in Study Patients: In this study, mild thrombocytopenia was most common, which was observed in 71 patients (54.6%), followed by moderate thrombocytopenia in 45 patients (34.6%), and severe thrombocytopenia in 14 patients (10.8%).

Limitations of the Study

- Single centre study
- Smaller sample size

CONCLUSION

This study showed that females in the age group of 21 to 30 years were more commonly affected by Megaloblastic anaemia. Vegetarian diet can be one of the contributing factors for Megaloblastic anemia, as majority of Megaloblastic anaemia patients were vegetarian in this study. Fatiguability and pallor are the most common symptom and sign of Megaloblastic anaemia, irrespective of the etiology. Majority of patients with Megaloblastic anaemia demonstrated severe anemia with mild leukopenia and mild thrombocytopenia.

REFERENCES

1. Addison T. Anaemia—disease of the suprarenal capsules. London Med Gazette. 1849; 43: 517–18.
2. Carmel R. Megaloblastic anemias: Disorders of impaired DNA synthesis. Wintrobe's clinical hematology. 2004; 11(1): 1367–95.
3. Antony AC. Megaloblastic anemia. Hematology. Basic principles and practice. 2009; 16 (2): 519–56.
4. Khanduri U, Sharma A. Megaloblastic anaemia: Prevalence and causative factors. Natl Med J India. 2007; 20:172-5