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Original Article

Clinico – Hematological Profile of Patients with Macrocytic Anemia

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ABSTRACT

Background: Macrocytic anaemia is a common haematological disorder with diverse etiologies, most commonly due to vitamin B12 and folate deficiencies. Early identification is essential to prevent complications, especially neurological damage.
Objectives: To evaluate the clinico-haematological profile and etiological factors of macrocytic anaemia in patients attending a tertiary care hospital.
Methods: This hospital-based cross-sectional observational study was conducted at GCS Medical College and Hospital, Ahmedabad, from November 2023 to March 2025. A total of 168 adult patients diagnosed with macrocytic anaemia (MCV >100 fL) were included. Detailed clinical history, examination, and laboratory investigations, including complete hemogram, peripheral smear, vitamin B12, folate levels, and other relevant tests, were performed. Data were analysed using SPSS software.
Results: The majority of patients were in the 41–60 years age group, with a slight male predominance. Common symptoms included dyspnea (26.2%) and fatigability (20.2%). A high proportion (89.9%) followed a vegetarian diet. Vitamin B12 deficiency (46.4%) was the most common aetiology, followed by folate deficiency (37.5%). The mean haemoglobin was 8.53 g/dL and the mean MCV was 105.49 fL. Cytopenias were frequently observed, with bicytopenia being more common than pancytopenia. Peripheral smear showed macrocytosis in all cases, along with anisocytosis and poikilocytosis.
Conclusion: Macrocytic anaemia in this population is predominantly nutritional in origin, especially due to vitamin B12 deficiency. Early diagnosis and prompt treatment are essential to prevent complications and improve patient outcomes.

Keywords*: Macrocytic anaemia, Vitamin B12 deficiency, Folate deficiency, Megaloblastic anaemia, Cytopenia.*

INTRODUCTION

Macrocytic anaemia is a haematological disorder characterised by enlarged red blood cells with an increased mean corpuscular volume (MCV >100 fL). It represents a heterogeneous group of conditions with varied etiologies, ranging from nutritional deficiencies to systemic diseases and bone marrow disorders (1).

The most common causes of macrocytic anaemia are deficiencies of vitamin B12 and folic acid, which result in defective DNA synthesis and ineffective erythropoiesis, leading to megaloblastic anaemia (2). These deficiencies are particularly prevalent in developing countries due to poor nutritional intake, malabsorption syndromes, and dietary practices such as strict vegetarianism (3).

Vitamin B12 plays a crucial role in DNA synthesis and neurological function. Its deficiency leads to both haematological abnormalities and neurological manifestations such as paresthesia and cognitive impairment (4). Folic acid deficiency, although primarily haematological in presentation, is commonly associated with poor diet, alcoholism, and increased metabolic demands (5).

In addition to nutritional causes, macrocytic anaemia may arise from non-megaloblastic conditions such as chronic liver disease, hypothyroidism, alcoholism, and drug-induced marrow suppression (6). Alcohol contributes to macrocytosis through direct toxic effects on the bone marrow and interference with folate metabolism (7).

Peripheral smear examination plays an essential role in the diagnosis of macrocytic anaemia. Classical findings include macro-ovalocytes, anisocytosis, poikilocytosis, and hypersegmented neutrophils (8). In severe cases, ineffective hematopoiesis can lead to cytopenias such as bicytopenia and pancytopenia (9).

Early identification of the underlying cause is critical, as many forms of macrocytic anaemia are reversible with appropriate therapy. However, delayed diagnosis, particularly in vitamin B12 deficiency, may result in irreversible neurological damage (10).

Despite its clinical significance, there is limited comprehensive data regarding the clinico-haematological profile of macrocytic anaemia in tertiary care settings. Therefore, the present study was undertaken to evaluate the clinical presentation, haematological parameters, and etiological spectrum of macrocytic anaemia.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, cross-sectional observational study conducted at GCS Medical College and Hospital, Ahmedabad.

Study Period

The study was carried out over a period of 17 months, from November 2023 to March 2025.

Sample Size Calculation

The sample size was calculated based on the prevalence of macrocytic anaemia obtained from a pilot study, which was found to be 12%. The sample size was determined using the formula:

$$n = \frac{Z^2 \times p \times q}{L^2}$$

Where:

- p = prevalence of macrocytic anemia = 12% (0.12)
- q = 1 − p = 88% (0.88)
- L = allowable error = 5% (0.05)
- Z = 1.96 (for 95% confidence interval)

The calculated sample size was approximately 162. To account for possible dropouts and incomplete data, the final sample size was rounded to 168 patients.

Study Population

The study population included all patients admitted or attending the outpatient department (OPD) or inpatient department (IPD) of the tertiary care hospital who were diagnosed with macrocytic anaemia.

Inclusion Criteria

1. Adult patients (≥18 years) diagnosed with macrocytic anaemia, defined as:
    - Mean corpuscular volume (MCV) > 100 fL
    - Hemoglobin level < 13 g/dL in males and < 12 g/dL in females
2. Patients attending OPD or admitted to the hospital
3. Patients who provided informed consent

Exclusion Criteria

1. Patients below 18 years of age
2. Pregnant women
3. Patients already receiving treatment that could affect study outcomes (e.g., vitamin supplementation, chemotherapy)
4. Patients unwilling to provide informed consent

Data Collection and Study Variables

A detailed clinical history was obtained from all enrolled patients, including demographic details, dietary habits, alcohol intake, drug history, and associated comorbidities such as thyroid disorders and chronic illnesses.
A thorough general and systemic clinical examination was performed in all cases.

Laboratory Investigations
All patients underwent the following investigations:

- Complete hemogram, including hemoglobin, red blood cell indices (MCV, MCH, MCHC), red cell distribution width (RDW), total and differential leukocyte count, platelet count, and reticulocyte count
- Serum lactate dehydrogenase (LDH)
- Peripheral blood smear examination

In patients with features suggestive of megaloblastic anaemia (such as macro-ovalocytes and hypersegmented neutrophils), bone marrow aspiration and biopsy were performed after obtaining informed consent.

Additional investigations included:

- Liver function tests in patients presenting with jaundice
- Serum thyroid-stimulating hormone (TSH) levels to assess thyroid dysfunction
- Serum vitamin B12 and folate levels (measured in fasting state)

An upper gastrointestinal endoscopy with biopsy from the second part of the duodenum was performed in selected patients with megaloblastic anaemia who consented to the procedure.

Statistical Analysis
Data were entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) software. Categorical variables were expressed as frequencies and percentages. Continuous variables were summarised as mean and standard deviation. Appropriate statistical tests were applied wherever necessary, and results were presented in tables and figures.

Ethical Considerations
Ethical approval for the study was obtained from the Institutional Ethics Committee of GCS Medical College and Hospital, Ahmedabad. Written informed consent was obtained from all participants prior to inclusion in the study. Confidentiality of patient information was strictly maintained throughout the study.

RESULT AND OBSERVATIONS

Table 1: Age and Sex Distribution of Study Subjects

Age Group (Years)	Male (n)	Female (n)	Total (n)	Percentage (%)
≤20	3	2	5	3.0%
21–40	30	25	55	32.7%
41–60	31	25	56	33.3%
60–80	24	27	51	30.4%
>80	1	0	1	0.6%
Total	**89**	**79**	**168**	**100.0%**

Table 2 : Presenting Complaints and Clinical Findings of Study Subjects

Variable Type	Parameter	No.	Percentage (%)
Complaints	Dyspnea	44	26.2%
	Fatiguability	34	20.2%
	Paresthesia	20	11.9%
	Pedal edema	18	10.7%
	Vomiting	18	10.7%
	Diarrhoea	17	10.1%
	Constipation	5	3.0%
	Abdominal pain	3	1.8%
	Bleeding	3	1.8%
	Pedal edema + dyspnea	3	1.8%
	Fever	2	1.2%
	Decreased appetite	1	0.6%
Clinical Findings	Organomegaly	125	74.4%
	Tachycardia	84	50.0%
	Pedal edema	62	36.9%
	Pallor	58	34.5%
	Glossitis	21	12.5%
	BMI ≥30	15	8.9%
	Skin hyperpigmentation	7	4.2%

Table 3: Personal History, Past History, and Etiology of Study Subjects

Variable Type	Parameter	No.	Percentage (%)
Personal History	Only vegetarian diet	151	89.9%
	Alcohol consumption	43	25.6%
	Smoking	35	20.8%
Past History	PCV transfusion	19	11.3%
Etiology	Vitamin B12 deficiency	78	46.4%
	Folate deficiency	63	37.5%

Table 4: Hematological Profile in study subjects

Hematological Profile	Mean	SD
Hb	8.53	2.48
TLC	7736.00	7122.22
Platelet	175333.33	93708.47
MCV	105.49	5.26
MCH	29.49	2.88
MCHC	33.03	1.17
Retic Count	1.13	1.33
RDW	19.34	3.79
Vit. B12	326.33	167.65
LDH	835.11	454.62
Folic acid	3.90	2.14
Homocystiene Level	18.45	4.01
TSH	4.08	4.00
S. bilirubin Total	1.73	1.39
S. bilirubin Direct	0.75	0.70

Table 5: Cytopenia vs Sex in study subjects

	Male		Female	
	No.	Percentage	No.	Percentage
Pancytopenia	16	9.5%	4	2.4%
Bicytopenia	46	27.4%	15	8.9%

Table 6: Haematological Parameters in Cytopenia and Haemoglobin–MCV Distribution by Sex

A. Haematological Parameters in Cytopenia

Parameter	Pancytopenia (Mean ± SD)	Bicytopenia (Mean ± SD)
Haemoglobin (Hb)	6.04 ± 1.67	6.52 ± 1.80
TLC	2980.00 ± 581.83	—
Platelet Count	84650.00 ± 22422.44	87590.16 ± 24515.56

B. Haemoglobin and MCV Distribution According to Sex

Haemoglobin (g/dL)	MCV (Mean ± SD)	Male (n)	Male (%)	Female (n)	Female (%)
<6	109.40 ± 10.12	17	10.1%	8	4.8%
≥6	104.81 ± 3.47	72	42.9%	71	42.3%

Table 7: Mean Vit B12 level and cytopenia

	MCV		Vit B12 Deficiency		Folic Acid Deficiency	
	Mean	SD	No.	Percentage	No.	Percentage
Pancytopenia	105.90	3.37	13	65.0%	9	45.0%
Bicytopenia	106.62	7.35	30	49.2%	25	41.0%
Anemia	104.76	3.51	37	40.7%	32	35.2%

Table 8: Peripheral smear in study subjects

Peripheral Smear	No.	Percentage
Macrocytes	168	100%
Hypersegmented neutrophils	39	23.2%
Anisocytosis	161	95.8%
Poikilocytosis	151	89.9%
Ovalocytes	141	83.9%

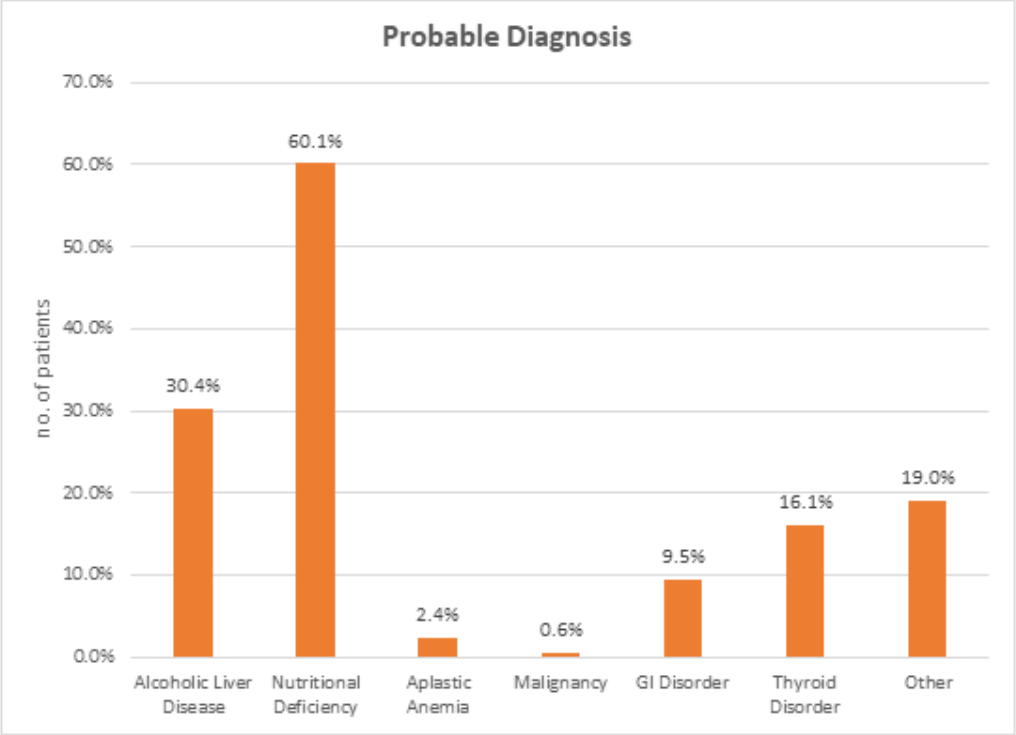

Figure 1: Aetiology of macrocytic anaemia

DISCUSSION

Macrocytic anemia is a clinically important condition with diverse etiologies and presentations. The present study evaluated 168 patients and provides valuable insights into the demographic, clinical, and hematological characteristics of macrocytic anemia in a tertiary care setting.

In this study, the majority of patients were in the middle-aged and elderly groups, particularly in the 41–60 years age group. This finding is consistent with previous studies indicating that macrocytic anemia is more prevalent in adults due to cumulative nutritional deficiencies and chronic illnesses (11).

A slight male predominance was observed, which may be attributed to higher exposure to risk factors such as alcohol consumption and smoking among males. Similar findings have been reported in other studies (12).

The most common presenting complaints were dyspnea and fatigability, reflecting reduced oxygen-carrying capacity. Neurological symptoms such as paresthesia were also noted, which are characteristic of vitamin B12 deficiency (13).

Clinical examination revealed organomegaly, tachycardia, and pedal edema as the most frequent findings, indicating chronicity and systemic involvement. Classical signs such as glossitis and hyperpigmentation further support the diagnosis of megaloblastic anemia (14).

A high prevalence of vegetarian diet was observed in this study. Since vitamin B12 is primarily derived from animal sources, strict vegetarianism is a major risk factor for deficiency, especially in the Indian population (15). Alcohol consumption was also noted as a contributing factor due to its effect on bone marrow and folate metabolism (16).

Vitamin B12 deficiency was identified as the most common etiological factor, followed by folate deficiency. These findings are consistent with studies conducted in developing countries, where nutritional deficiencies predominate (17).
The hematological profile demonstrated moderate anemia with elevated MCV, confirming macrocytosis. Increased RDW and elevated LDH levels indicated ineffective erythropoiesis and red cell destruction (18).

Cytopenias were frequently observed, with bicytopenia being more common than pancytopenia. Patients with pancytopenia showed more severe hematological abnormalities, indicating advanced marrow involvement (19).

A clear association was noted between the severity of anaemia and the degree of macrocytosis, with more severe anaemia showing higher MCV values. Vitamin B12 deficiency was most prevalent among patients with pancytopenia, highlighting its role in severe haematological derangements.

Peripheral smear findings were characteristic, showing macrocytosis in all cases along with anisocytosis, poikilocytosis, and ovalocytes. Hypersegmented neutrophils, although less frequent, remain a hallmark feature of megaloblastic anaemia (20).

Overall, the findings emphasise that macrocytic anaemia in this population is predominantly due to nutritional deficiencies, particularly vitamin B12 deficiency. Early diagnosis and timely treatment are essential to prevent complications, especially irreversible neurological damage (21).

CONCLUSION

Macrocytic anaemia in this study predominantly affected middle-aged and elderly individuals, with a slight male predominance. The most common presentations were dyspnea and fatigability, with occasional neurological symptoms.

Vitamin B12 deficiency was the leading cause, followed by folate deficiency, largely associated with a vegetarian diet and alcohol use. Haematological findings showed moderate anaemia with macrocytosis, and cytopenias were common, especially in severe cases.

Overall, macrocytic anaemia is mainly nutritional in origin, and early diagnosis with timely treatment is essential to prevent complications, particularly neurological damage**.**

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