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Original Research Article

Deciphering Macrocytic Anemia: Insights into Etiology and Hematology from South Rajasthan

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Abstract:

Introduction: Macrocytosis characterized by abnormally large erythrocytes with an increase mean corpuscular volume (MCV), is a hematological condition indicative of various underlying pathologies. It is clinically significant and can range from nutritional deficiencies to bone marrow disorders. The prevalence in India varies significantly, making a complete workup essential for determining its etiology.

Material and Method: This retrospective study from May to October 2023 in South Rajasthan, India, included 142 cases. It utilized clinical history, peripheral blood film examination, and biochemical tests for diagnosis.

Result: Vitamin B12 deficiency was the most common (55.63%) cause of megaloblastic macrocytic anemia and alcohol was the most common (14.79%) cause of nonmegaloblastic macrocytic anemia in this study.

Conclusion: The present study suggests that vitamin B12 deficiency, alcoholism, liver disease, and drugs were the main causes of macrocytic anemia in South Rajasthan, India. The study suggests that haematological parameters along with clinical history, peripheral smear examination and biochemical analysis is useful tools for detecting and managing macrocytosis.

Keywords: Macrocytosis, Anemia, Vitamin B12 deficiency, Nutritional Deficiencies, Hematology.

Introduction

Macrocytosis, characterized by the presence of abnormally large erythrocytes with an increased mean corpuscular volume (MCV) in peripheral blood smears, is a haematological condition that can be indicative of various underlying pathologies [1]. The definition of macrocytosis is typically operationalized with an MCV exceeding 100 femtolitres (fl), diverging from the normal adult range of 80-100 fl [2]. The clinical significance of macrocytosis extends beyond a mere laboratory finding; it can be a crucial indicator of diverse clinical conditions, ranging from nutritional deficiencies to bone marrow disorders [1]. The prevalence of macrocytosis varies in India, with studies reporting an incidence between 02% and 40% in different populations [3].

Variety of known and postulated mechanisms are responsible for the disorder that leads to macrocytic anaemia. Based on the mechanism they are generally classified into two groups. (A) megaloblastic macrocytic anemia (due to disorders in DNA synthesis of erythrocyte precursors in the bone marrow), (B) non-megaloblastic macrocytic anemia (caused by variety of other mechanisms) [4].

physiological macrocytosis is seen in pregnancy, newborns and infants. In some genetic conditions macrocytosis without anemia may be found as a normal variant. False elevation of MCV also found in hyperglycaemia, cold agglutinins, reticulocytosis, leukocytosis and delayed sample processing [5].

Causes of macrocytosis are many, thus a complete workup is essential to determine its etiology [6]. Etiological factors contributing to macrocytosis include nutritional deficiencies (notably vitamin B12 and folate deficiency), alcoholism, medication effects, and hematological conditions such as myelodysplastic syndromes. The presence of macrocytosis without accompanying anemia is a diagnostic challenge, observed in approximately 60% of cases in some studies. This subset of macrocytosis necessitates careful evaluation due to the potential masking of underlying conditions [7].

Blood profile can be defined directly by haematological indices like Hb, MCV, MCH, MCHC and Red cell distribution width. These parameters are also used for define type of anemia. High MCV values are indicative of macrocytic anemia, peripheral smear examination required for confirmation [8]. In megaloblastic anemia presence of macro-ovalocytes is a sensitive finding but the presence of hypersegmented neutrophils is more specific [1].

In South Rajasthan of India, specific data on the prevalence and causes of macrocytosis is scarce. This study aims to analyse these aspects in a tertiary care setting, offering insights into the haematological profile of macrocytosis in this region. By doing so, it contributes to the broader understanding of macrocytosis in the Indian context, emphasizing its clinical implications and guiding effective management strategies.

Material and Method

This was a retrospective study, spanning six months from May 2023 to October 2023. It will be conducted in a tertiary care hospital in South Rajasthan, India, which serves a diverse patient population. This setting is suitable for understanding the regional prevalence and characteristics of macrocytosis.

Inclusion Criteria: Adult patients (age ≥13 years) undergoing routine blood tests or presenting with symptoms indicative of anemia was included.

Exclusion Criteria: Pregnant women, Newborns and infants were excluded from the study.

- Patients with finding of reticulocytotic, hyperglycaemia, presence of cold agglutinins, leukocytosis, delay in processing of sample.
- Macrocytosis cases where underlying aetiology was not identified were also not included in the study.

Macrocytosis was identified in patients whose CBC finding shows an MCV of >100 fl. Data on patients' demographic details, clinical history, and specific symptoms was collected from hospital records. Automated haematology analysers was used for complete blood counts, including red blood cell indices like MCV, MCH, and RDW. Cases with Hb<11.5 g/dl (females) and Hb<12.5 g/dl (males) were considered anemic. Peripheral blood smears will be prepared and examined for signs of macrocytosis. Reticulocyte count was performed in presence of polychromasia, nucleated RBCs, spherocytes, schistocytes or any condition leading to acute bleed or haemolysis.

Where necessary, biochemical analysis (e.g., Vitamin B12 and folate assays) was conducted to differentiate between megaloblastic and nonmegaloblastic macrocytosis. For certain cases, more advanced diagnostics, such as bone marrow examination was done.

The data was be analysed using retrospective statical analysis. The prevalence of macrocytosis and associated conditions was calculated, and associations with demographic and clinical parameters was explored.

Result

During the one-year study period from May 2023 to October 2023, a total of 142 patients underwent complete blood count (CBC) analysis and were identified with macrocytosis (after applying all exclusion criteria), characterized by an MCV greater than 100 femtolitres.

The demographic distribution of the patients with macrocytosis showed a 60.56% prevalence in males and 39.44% in females. The age range of the patients varied from 13 - 68 years, with the majority falling within the 21-30 age group.

The most common cause of macrocytosis identified was vitamin B12 deficiency, found in 79 cases (55.63%). This was followed by alcoholism, observed in 21 cases (14.79%), followed by liver disease observed in 16 cases (11.27%) and drug intake contributing to 14 cases (9.86%). Additionally, 9 cases (6.33%) of macrocytosis were noted to occur due to combined vit B12 and Folate deficiency. Only 2 cases (1.41%) were due to Myelodysplastic syndrome and only 1 case (0.71%) was due to aplastic anemia. (Table No. 1)

Table No. 1: Factors responsible for macrocytosis

S. No.	Etiological factor	No. of cases	Percentage
1	Vit B12 deficiency	79	55.63
2	Alcoholism	21	14.79
3	Drug related	14	9.86
4	Aplastic anemia	1	0.71
5	Combined vit B12 and Folate deficiency	9	6.33
6	Liver disease	16	11.27
7	Myelodysplastic syndrome	2	1.41
	Total	142	100

In terms of hematological features, the presence of hypersegmented neutrophils and macro-ovalocytes was frequently observed in peripheral blood smear examinations, especially in patients with megaloblastic conditions. The average MCV in patients with macrocytosis was 122.1 fl. In cases of macrocytosis due to alcoholism, the MCV ranged up to 114.5 fl, while in vitamin B12 deficiency, it went up to 143.6 fl. The mean red cell distribution width (RDW) in megaloblastic cases was 28.7%, compared to 20% in nonmegaloblastic cases. (Table No. 2)

Table No. 2: Hematological parameters

S. No.	Parameters	Megaloblastic (88 cases)	Non-megaloblastic category (54 cases)
1	Hb (g/dl)	8.6 (2.4-12.5)	9.65 (6.1-13.2)
2	MCV (fl)	122.1 (100.6-143.6)	107.2 (100-114.5)
3	MCH (pg)	37.95 (28.8-47.1)	35.5 (31.4-39.6)
4	Red cell count (x1012/l)	2.36 (0.51-4.21)	3.87 (2.4-5.34)
5	RDW-CV%	28.7% (12.5-44.9)	20% (12.4-27.6)
6	TLC (x10-9/l)	5.67 (1.14-10.2)	9.4 (2.1-16.7)
7	Platelet count (x10-9/l)	276 (16-546)	354.5 (56-653)
8	Hypersegmented neutrophils	86%	10.2%
9	Macro-ovalocytes	87.3%	12.8%

Discussion

In the present study the demographic distribution of the patients showed a 60.56% prevalence in males and 39.44% in females with macrocytosis. Gupta et al. demonstrate 65.17% prevalence of macrocytosis in male [8]. Study done by Jitendra et al. in northern India shows 52.27% prevalence in male [9].

Present study shows most common etiological factor for macrocytosis is Vit B12 deficiency (55.63% cases). Study done by Khanduri et al. also shows most common cause of macrocytosis was cobalamin deficiency in 78 patients (65% cases) [10]. Iqbal et al. also shows vitamin B12 deficiency was 78.5% in these patients [11]. In this study, among nonmegaloblastic, most common cause of macrocytosis is alcohol intake was detected in 21 cases (14.79%). Study done by Savage et al. demonstrate drug intake and alcoholism was the most common causes [12]. Unnikrishnan V et al. observed Vit B12 deficiency and alcoholism as the most frequent causes [4].

Present study shows 9.86% cases of macrocytic anemia was drug related. some of the known drugs that causing macrocytosis are anticonvulsants, chemotherapeutics agents, sulfasalazine, folate antagonists, antiretroviral drugs, sulfamethoxazole, pyrimethamine, trimethoprim, metformin [13,14].

Average value of MCV is 122.1 fl found in megaloblastic macrocytic cases of the present study. While MCV value of nonmegaloblastic cases range from 100 fl to 114.5 fl. Study done by Park et al. represent MCV between 100 fl to 110 fl in alcoholism [15]. Noora Saeed et al. shows mean MCV for megaloblastic cases was 112.2 fl and 106.9 fl for nonmegaloblastic cases [1].

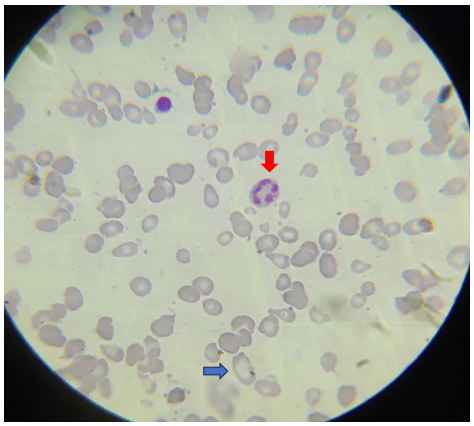

Figure 1: peripheral blood smear showing macro-ovalocytes (blue arrows), hypersegmented neutrophil (red arrows), anisocytosis in a case of vitamin B12 deficiency

Peripheral blood examination shows presence of macroovalocyte and hypersegmented neutrophils in megaloblastic cases of this study. (Figure 1) Presence of macroovalocyte is sensitive while presence of hypersegmented neutrophils is a more specific finding in megaloblastic anemia [10]. However, presence of hypersegmented neutrophils is not definite finding, since they can be absent in shift to right or severe neutropenia [16].

Bone marrow aspirate in megaloblastic anemia is mostly cellular, showing varying degree

of dyserythropoiesis with megaloblasts, megakaryocytes, few giant forms of metamyelocytes and band forms which is similar to the findings in this study [12]. (Figure 2)

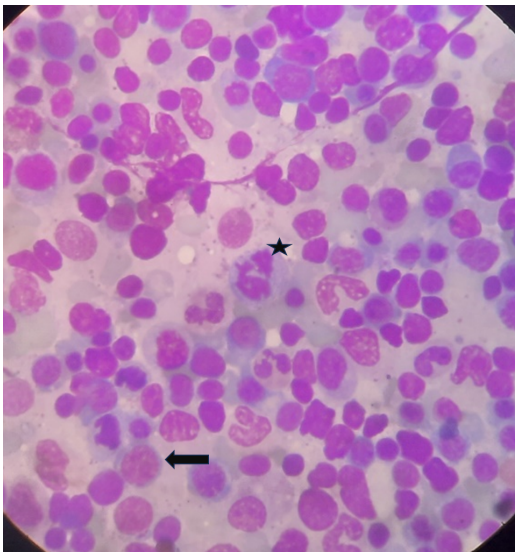

Figure 2: Bone marrow aspiration showing megaloblast having sieve like chromatin (black arrow) and features of dyserythropoiesis (star mark)

Conclusion

Vitamin B12 deficiency is a major factor causing macrocytic anemia. Apart that alcohol, liver disease and drugs are common cause. They can be easily rule out by haematological parameters. MCV more than 100 fl is a diagnostic clue for the evaluation of macrocytosis. In resource limited county like India haematological parameters along with clinical history, peripheral smear examination and biochemical analysis is inexpensive tools for detection of macrocytosis. However few cases require bone marrow aspiration study for confirmation of diagnosis.

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