Orginal Article

Etiological Profile of Macrocytic Anemia in Patients Attending a Tertiary Care Hospital in Nepal

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Abstract

Introduction: The morphological classification of anemia often correlates with the cause of red cell deficiency. Megaloblastic and non-megaloblastic macrocytic anemias are important causes of anemia in at least 1.7% of hospital patients. Vitamin B12 and folate deficiency are rampant in underdeveloped countries. In Nepal, there is a lack of local data evaluating the etiological profile of macrocytic anemia.

Methods: A descriptive hospital-based study was conducted, and thirty-five cases of anemia according to the WHO criteria were included after informed consent. Clinical history, physical examination, complete hemogram (including hemoglobin level, red cell indices, total leucocyte count, platelet count, and reticulocyte count), and a peripheral blood smear were obtained per structured proforma. Appropriate biochemical investigations were acquired. Statistical analyses were performed as per standard statistical protocols.

Results: The mean age of the patients in our study was 42.40 (±10.29) years. There was a slight male predominance (n=20; 57.14%). Most cases (n=27;77.14%) of macrocytic anemia were megaloblastic. Vitamin B12 deficiency (n=13; 48.14%) was the commonest identifiable cause in megaloblastic group, while liver disease accounts for half of the cases (n=4; 50%) of non-megaloblastic group. The mean hemoglobin was lower (9.94±1.43 g/dl) in megaloblastic anemia compared to non-megaloblastic macrocytic anemia (10.96±1.24 g/dl).

Conclusion: The present study showed that megaloblastic anemia was the most common cause of macrocytic anemia, primarily due to vitamin B12 and folate deficiency. Non-megaloblastic anemia was mainly attributed to liver diseases.

Keywords: *Macrocytic anaemia, megaloblastic anaemia*

Introduction

Anemia is a significant but treatable health burden worldwide, with the global prevalence of anemia reaching 22.8% in 2019[1]. The World Health Organization (WHO) diagnostic criteria of anemia are hemoglobin concentration less than 13gm/dl in men and 12gm/dl in non-pregnant women[2].

There are several classifications of anemia; one is based on the underlying mechanism, and the other classifies anemia according to the alteration in red cell morphology. The latter classification often correlates with the cause of red cell deficiency. The morphological classification includes normocytic,

microcytic, and macrocytic anemia.

RBCs are microcytic if cells are smaller than normal and macrocytic if larger[3]. A mean corpuscular volume (MCV) of 80-100fl is the normal value. Macrocytic anemias are further classified as megaloblastic macrocytic anemias (MMA) and non-megaloblastic macrocytic anemia (NMA).

Worldwide the most common cause of anemia is microcytic anemia due to iron deficiency. Macrocytic anemia due to vitamin B12 and folic acid deficiency is also an important cause of anemia. Macrocytosis is seen in 1.7-3.6% of patients seeking medical care[4 5].

According to WHO, no accurate figures on the worldwide prevalence of megaloblastic anemia are available. Studies have been done only in a few countries and ethnic groups[6]. Macrocytic anemia was found in 7.5 % of patients with newly diagnosed anemia in general practice[7].

About 95% of megaloblastic anemias are due to vitamin B12 and folate deficiency, which is highest in countries with malnutrition and inadequa te vitamin supplementation[8]. NMA are caused by hemolysis, alcohol toxicity, hypothyroidism, liver disease, etc., whereas physiological macrocytosis is seen in neonates and pregnant women[4, 9].

The current hospital-based study was carried out due to the paucity of local data accessing the etiological profile of macrocytic anemia. Diagnosis of macrocytic anemia can be made with the help of clinical history, physical examination, and hematological profile, including hemoglobin, red cell indices, and relevant biochemical tests.

Methods

After obtaining approval from Institutional Review Committee (Reference No. 2077/78/74), a hospital-based prospective descriptive study was conducted for a period of one year from May 2021 to April 2022. Thirty-five cases of anemia according to the WHO criteria and macrocytosis (MCV>100 fl) were included in the study. Patients under 18 years, pregnant women, and those diagnosed with nutritional deficiency anemia under treatment were excluded. Informed consent was obtained from the patient.

Clinical history and a complete and thorough physical examination were carried out. The history was sought, emphasizing diet and alcohol consumption, present and previous illness, surgery, and drug intake.

A complete hemogram was obtained, including hemoglobin level, MCV, mean corpuscular hemoglobin (MCH), total leucocyte count, platelet count, reticulocyte count, and peripheral blood smear (PBS). Subsequently, in patients who have hematological evidence of macrocytosis, appropriate biochemical investigations like serum vitamin B12 and folate level, liver function test (LFT), thyroid function test (TFT), and iron profile were also acquired.

The obtained data were analyzed using IBM SPSS (version 24) per standard statistical protocol.

Results

A total of 35 patients with macrocytic anemia were recruited in our study. Amongst them, 27 (77.14%) cases were of megaloblastic type. The rest were non-megaloblastic type (n=8; 22.86%). The mean age of patients included in our study was 42.40 (±SD 10.29) years, with a range of 23-63 years. The mean age in the megaloblastic and non-megaloblastic groups was 41.67 (±SD 10.23) and 44.88 (±SD 10.80) years, respectively (p=.471). Males comprised most of our study subjects (n=20; 57.14%), whereas the rest were females (n=15; 42.86%). The majority of our patients were involved in the agriculture (n=10; 28.57%) or business (n=10; 28.57%) profession. Service industry professionals (n=7; 20%), housewives (n=6; 17.14%), and students (n=2; 5.71%) comprised the rest. The most common presenting symptom and signs in macrocytic anemia cases were weakness (n=14; 40%) and pallor (n=24; 68.57%), respectively. (Table 1; Table 2)

Table 1: Presenting symptoms of macrocytic anemia

Symptom	Frequency (n)	Percentage (%)
Weakness	14	40.00
Incidental	6	17.14
Abdominal distension	2	5.71
Tingling Sensation	3	8.57
Burning Tongue	3	8.57
Decreased Appetite	7	20.00
Total	35	100

Table 2: Presenting signs of macrocytic anemia

Sign	Frequency (n)	Percentage (%)
Pallor	24	68.57
Hepatomegaly	3	8.57
Brittle nails	2	5.71
Glossitis	1	2.86
Splenomegaly	1	2.86
Hepatosplenomegaly	2	5.71
Icterus	2	5.71
Total	35	100

In our study, non-vegetarians and vegetarians comprised 24 (68.57%) and 11 (31.43%) cases, respectively. In the megaloblastic group, non-vegetarians (59.26%) and vegetarians comprised 16 and 11 (40.74%) cases, respectively. All cases (n=8; 100%) were non-vegetarians in the non-megaloblastic group. (Table 3)

Table 3: Dietary profile of macrocytic anemia

Type	Non-vegetarians (n)	Vegetarians (n)	Total
Megaloblastic (%)	16 (59.26)	11 (40.74)	27 (100)
Non-megaloblastic (%)	8 (100)	0	8 (100

The majority of macrocytic anemia cases were of megaloblastic type (n=27). Vitamin B12 deficiency (n=13; 48.14%) was the commonest identifiable cause in this group. Folate deficiency was present in seven cases (25.93%). (Table 4) Non-megaloblastic type of macrocytic anemia was identified in eight cases. The causes of non-megaloblastic type of macrocytic anemia were liver disease (n=4; 50%), alcoholism (n=3; 37.5%), and hypothyroidism (n=1; 12.5%).

Table 4: Etiology of megaloblastic type of macrocytic anemia

Etiology	Frequency (n)	Percentage (%)
Vitamin B12 deficiency	13	48.14
Folate deficiency	7	25.93
Vitamin B12 and Folate deficiency	3	11.11
Vitamin B12 and Iron deficiency	4	14.81
Total	27	100

The mean hemoglobin was lower (9.94±1.43 g/dl) in megaloblastic anemia compared to non-megaloblastic macrocytic anemia (10.96±1.24 g/dl). Higher mean MCV (108.01±4.98fl) was noted in patients of megaloblastic group, as compared to non-megaloblastic group (106.13±5.62 fl). Peripheral smears in patients with megaloblastic anemia revealed hypersegmented neutrophils in 15 patients (55.56%). In non-megaloblastic type, this finding was seen in none of the patients. (Table 5)

Table 5.Hematological profile in macrocytic anemia

Parameter	Megaloblastic anemia	Non-megaloblastic anemia
Hemoglobin (g/dl)	9.94 (±SD 1.43)	10.96 (±SD 1.24)
MCV[a] (fl)	108.01(±SD 4.98)	106.13 (±SD 5.62)
MCH[b] (pg)	33.63 (±SD 3.59)	33.50 (±SD 1.77)
TLC[c] (/mm3)	4485.19	5962.50
PLT[d] (/mm3)	155481.48	173750
Hypersegmented neutrophils (%)	55.56	0

[a] Mean Corpuscular Volume; [b] Mean Corpuscular Hemoglobin; [c] Total Leucocyte Count; [d] Platelet Count

Discussion

Hematological indices and morphological classification of anemia on peripheral blood smears are helpful adjuncts to clinical characteristics and biochemical parameters in classifying anemia and identifying the etiology. Macrocytic anemia is a distinct morphological subgroup defined by a considerable increase in red cell size.

The mean age of cases of macrocytic anemia differs in studies[5,7,10]. In our study, the mean age was 42.40 ± 10.29 years. Common disorders of aging may cause vitamin B12 deficiency, causing macrocytic anemia[4]. Additionally, local demographic factors may account for the observed differences. There was a slight male preponderance in the study (57.14%), which is comparable to the study by Unnikrishnan et al. and Stouten et al[5,7]. The predominant clinical findings in our study were pallor and weakness, similar to the study by Khanduri et al[10].

The reported causes of macrocytosis differ between studies, but alcoholism, vitamin B12 and folate deficiencies, and medications are the most frequent causes[10]. Vitamin B12 deficiency, folate deficiency, and liver diseases were the common causes of macrocytic anemia in this study. According to Unnikrishnan et al. vitamin B12 insufficiency is one of the most common etiological causes of megaloblastic anemia, which is consistent with the results of this study[5].

Our study also showed combined vitamin B12 and folate deficiency in 11.11% of the cases with megaloblastic anemia. Similar conclusions were also observed in the study by Kanduri et al. where combined deficiency was seen in 12% of the megaloblastic cases. Non-megaloblastic anemia is associated with liver disease, hypothyroidism, and bone marrow disorders[11]. In the present study, the cause of non-megaloblastic anemia was liver disease (50%), alcoholism (37.5%), and hypothyroidism (12.5%).

In our study, a sizable number of non-vegetarians (59.69%) had megaloblastic anemia. A similar finding was observed by Unnikrishnan et al. and Masalha et al[5,12]. Higher mean MCV (108.01±4.98fl) was noted in patients of megaloblastic group. The findings in this study also parallel with results of the study by Unnikrishnan et al[5].

Conclusion

The present study showed megaloblastic anemia is the most common cause of macrocytic anemia. The common causes identified were vitamin B12 and folate deficiency, along with liver diseases.

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