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Original Research Article

A Hospital-Based Study to Determine the Specific Aetiology of Microcytic Anemia: an Observational Study

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Abstract

Aim: To determine the specific cause of microcytic anemia in a tertiary care hospital.

Material and Methods: This study was conducted in the Department of pathology, ANMMCH, Gaya, Bihar, India from August 2019 to July 2020. Total 100 Cases of microcytic hypochromic anemias were taken from Outpatient Department and indoor. After taking written consent from all patient's workup was done according to seems etiology. The study was approved by the ethical committee of the institute. Age >18-year and Patient of microcytic hypochromic Anemia were included in this study.

Results: The etiological distribution of microcytic hypochromic anemia in the studied population revealed that iron deficiency anemia (IDA) was the most prevalent, affecting 61% of the participants. Anemia of chronic disease (AOCD) accounted for 28% of the cases, while thalassemia was identified in 11% of the subjects. Among the cases of AOCD, tuberculosis was the leading cause, responsible for 39.29% of the cases. This was followed by chronic kidney disease (10.71%), systemic lupus erythematosus (10.71%), rheumatoid arthritis (7.14%), diabetes mellitus (7.14%), multiple myeloma (7.14%), chronic lymphocytic leukemia (3.57%), non-Hodgkin lymphoma (3.57%), Hodgkin lymphoma (3.57%), lung carcinoma (3.57%), and Crohn's disease (3.57%). In the thalassemia group, the majority were diagnosed with thalassemia trait, which constituted 81.8% of the cases. Delta B thalassemia and double heterozygote HBE and B-thalassemia each accounted for 9% of the cases. The mean corpuscular indices revealed significant differences among the groups. The mean corpuscular volume (MCV) was highest in the IDA group (24.2115±7.25806 fL), followed by AOCD (15.5786±2.49345 fL), and lowest in thalassemia (13.5073±3.30384 fL) with a p-value of <0.001. The red cell distribution width (RDW) was significantly higher in IDA (19.466±1.9141%) compared to AOCD (15.650±1.3304%) and thalassemia (15.409±1.0222%) with a p-value of <0.001.

Conclusion: Anemia is not an illness in and of itself, but rather a symptom of another, hence finding the underlying cause is significantly more important. People suffering from chronic illnesses, which form a large group as a result of nutritional insufficiency and anaemia from chronic diseases, can be avoided to some extent by the ongoing and uninterrupted implementation of anti-tuberculosis programmes in third-world countries such as India.

Keywords: Iron deficiency anemia, Microcytic anemia.

Introduction

Microcytic anemia is characterized by the presence of abnormally small red blood cells (RBCs) with reduced hemoglobin content. This condition is commonly identified by a mean corpuscular volume (MCV) of less than 80 femtoliters. The differential diagnosis of microcytic anemia is broad, encompassing a variety of underlying causes, each with distinct pathophysiological mechanisms. The most prevalent causes include iron deficiency anemia (IDA), anemia of chronic disease (AOCD), and thalassemia. Each of these conditions requires specific diagnostic approaches and management strategies to address the underlying etiology effectively. Iron deficiency anemia is the most common form of microcytic anemia globally. It occurs due to insufficient iron intake, increased iron loss, or impaired iron absorption. The condition is often associated with chronic blood loss, particularly from the gastrointestinal tract or menstruation in women . [1-3] In IDA, iron studies typically reveal low serum iron, ferritin, and transferrin saturation, with an elevated total iron-binding capacity (TIBC).

The treatment focuses on identifying and addressing the source of blood loss and supplementing with oral or intravenous iron . Anemia of chronic disease, also known as anemia of inflammation, is the second most common cause of microcytic anemia. It is typically seen in patients with chronic infections, inflammatory diseases, or malignancies. The pathophysiology involves the sequestration of iron in macrophages and the suppression of erythropoiesis due to the effects of inflammatory cytokines. Unlike IDA, iron studies in AOCD show normal or increased ferritin levels and decreased TIBC, reflecting the body's attempt to limit iron availability to pathogens . Management of AOCD involves treating the underlying chronic condition and, in some cases, the use of erythropoiesis-stimulating agents (ESAs) . Thalassemia is a hereditary hemoglobinopathy resulting from mutations in the globin genes, leading to reduced or absent production of globin chains. The condition is prevalent in regions where malaria was or is endemic, as thalassemia confers a survival advantage against malaria. Thalassemia major, intermedia, and minor represent a spectrum of disease severity based on the number of affected globin genes. [4-7] Patients with thalassemia typically present with microcytosis and hypochromia, with or without anemia. Hemoglobin electrophoresis and genetic testing are essential for diagnosis. Management varies from regular blood transfusions and iron chelation therapy in severe cases to monitoring in asymptomatic carriers . Less common causes of microcytic anemia include sideroblastic anemia, lead poisoning, and certain chronic diseases. Sideroblastic anemia is characterized by defective heme synthesis within the mitochondria, leading to the presence of ringed sideroblasts in the bone marrow. Lead poisoning interferes with several enzymatic steps in the heme synthesis pathway, leading to microcytic anemia and basophilic stippling of erythrocytes . Additionally, certain chronic diseases such as hypothyroidism and chronic kidney disease can contribute to the development of microcytic anemia through various mechanisms. [8-10]

Material and Methods

This study was conducted in the Department of pathology, ANMMCH, Gaya, Bihar, India from August 2019 to July 2020. Total 100 Cases of microcytic hypochromic anemias were taken from Outpatient Department and indoor. After taking written consent from all patients workup was done according to seems etiology. The study was approved by the ethical committee of the institute. Age >18-year, Patient of microcytic hypochromic Anemia were included in this study. Age<18 years, Patient who refuses to consent, Anemia not caused by microcytic hypochromic anaemia. Microcytic anaemia aetiologies are evaluated by sending complete haematological investigations such as complete blood count, reticulocyte count, peripheral blood smears, serum iron, total iron binding capacity (TIBC), ferritin, haemoglobin electrophoresis, LDH, stool for occult blood and ova, cysts, liver and renal function. Proctoscopy, anti-tissue transglutaminase/antigliadin antibody, upper GI endoscopy, lower GI endoscopy, bone marrow examination including iron staining, Xray, abdominal ultrasonography, computed tomography abdominal scans were performed on selected patients based on their symptoms were excluded from the study.

Statistical Analysis

The statistical analysis was performed using statistical package for the social sciences (SPSS), Version 24.0. IBM Corp., NY). Simple descriptive statistics was used (mean ± standard deviation for quantitative variables, and frequency with percentage distribution for categorized variables). The statistical analysis was carried out for various categorical parameters using the chi-square test and Fischer's Exact Test. For comparing two groups of mean or median Student's t-test and Mann Whitney U test was performed. P-value <0.05 is considered as statistically significant.

Results

The etiological distribution of microcytic hypochromic anemia in the studied population revealed that iron deficiency anemia (IDA) was the most prevalent, affecting 61% of the participants. Anemia of chronic disease (AOCD) accounted for 28% of the cases, while thalassemia was identified in 11% of the subjects, as depicted in Table 1.

Among the cases of AOCD, tuberculosis was the leading cause, responsible for 39.29% of the cases. This was followed by chronic kidney disease (10.71%), systemic lupus erythematosus (10.71%), rheumatoid arthritis (7.14%), diabetes mellitus (7.14%), multiple myeloma (7.14%), chronic lymphocytic leukemia (3.57%), non-Hodgkin lymphoma (3.57%), Hodgkin lymphoma (3.57%), lung carcinoma (3.57%), and Crohn's disease (3.57%), as shown in Table 2.

In the thalassemia group, the majority were diagnosed with thalassemia trait, which constituted 81.8% of the cases. Delta B thalassemia and double heterozygote HBE and B-thalassemia each accounted for 9% of the cases, as seen in Table 3.

Gender distribution analysis across different diagnoses showed significant variation. Among the IDA group, females were more affected, constituting 65.6% of the cases compared to 34.4% in males. Conversely, in the AOCD group, males were more frequently affected, making up 57.1% of the cases compared to 42.9% in females. Thalassemia was

predominantly seen in females, comprising 81.8% of the cases, with only 18.2% in males. The chi-square test indicated a significant association between gender and diagnosis ($\chi 2=6.414$; p=0.040), as presented in Table 4.

The hemogram parameters varied significantly across the different types of anemia. The mean hemoglobin (HB) levels were lowest in the IDA group (6.97±1.5966 g/dL), followed by AOCD (7.80±1.1512 g/dL), and highest in the thalassemia group (8.00±0.9571 g/dL) with a p-value of 0.012. The total red blood cell count (TRBC) was also significantly different, being lowest in IDA (3.0123±0.72770 million cells/µL) and highest in thalassemia (4.8591±0.95264 million cells/µL) with a p-value of <0.001. Platelet counts (PLT) were highest in the IDA group (3.2170±1.30404 lakh/µL) and lowest in the thalassemia group (2.1109±0.62266 lakh/µL), with a significant p-value of 0.002, as detailed in Table 5.

The mean corpuscular indices revealed significant differences among the groups. The mean corpuscular volume (MCV) was highest in the IDA group (24.2115±7.25806 fL), followed by AOCD (15.5786±2.49345 fL), and lowest in thalassemia (13.5073±3.30384 fL) with a p-value of <0.001. The red cell distribution width (RDW) was significantly higher in IDA (19.466±1.9141%) compared to AOCD (15.650±1.3304%) and thalassemia (15.409±1.0222%) with a p-value of <0.001, as shown in Table 6.

The distribution of patients based on outpatient department (OPD) and inpatient department (IPD) visits also varied across diagnoses. In the IDA group, 44.3% were managed as outpatients, while 55.7% required inpatient care. For AOCD, a higher proportion of patients were managed as inpatients (71.4%) compared to outpatients (28.6%). In contrast, the majority of thalassemia cases were managed on an outpatient basis (81.8%), with only 18.2% requiring inpatient care, as detailed in Table 7.

Table 1: Etiological Distribution of Microcytic Hypochromic Anemia in Different Groups

Diagnosis	No.	%
Iron deficiency anemia (IDA)	61	61.0
Anemia of chronic disease (AOCD)	28	28.0
Thalassemia	11	11.0
Total	100	100.0

Table 2: Etiology of Anemia of Chronic Disease

Etiology	No.	%
Tuberculosis	11	39.28571
Chronic Kidney Disease	3	10.71429
Systemic lupus erythematous	3	10.71429
Rheumatoid arthritis	2	7.142857
Diabetes Mellitus	2	7.142857
Multiple Myeloma	2	7.142857
Chronic lymphocytic leukemia	1	3.571429
Non-Hodgkin lymphoma	1	3.571429
Hodgkin lymphoma	1	3.571429
Carcinoma Lung	1	3.571429
IBD - Crohn disease.	1	3.571429

Table 3: Etiology of Thalassemia

Type	No.	%
Thalassemia trait	9	81.8
Delta B thalassemia	1	9.0
Double heterozygote HBE and B- thalassemia	1	9.0

Table 4: Gender vs	**Diagnosis**						
Gender	IDA			DX AOCD			Thalassemia
	No.	%	No.		%	No.	%
Male	21	34.4	16		57.1	2	18.2
Female	40	65.6	12		42.9	9	81.8
Total	61	100	28		100	11	100
$\chi^2=6.414^a$; p=0.040							

Table 5: Hemogram

	IDA Mean±SD N=61	AOCD Mean±SD N=28	Thalassemia Mean±SD N=11	p-value
HB	6.970±1.5966	7.800±1.1512	8.000±0.9571	0.012
TRBC	3.0123±0.72770	3.8961±0.60399	4.8591±0.95264	<0.001
PLT	3.2170±1.30404	2.5679±0.72982	2.1109±0.62266	0.002

Table 6: Hemoglobin Indices

	IDA Mean±SD N=61	AOCD Mean±SD N=28	Thalassemia Mean±SD N=11	p-value
MI	24.2115±7.25806	15.5786±2.49345	13.5073±3.30384	<0.001
RDW	19.466±1.9141	15.650±1.3304	15.409±1.0222	<0.001

Table 7: Outpatient Department (OPD) / In-Patient Department (IPD) vs Diagnosis

OPD/IPD	No.	IDA	%	No.	Diagnosis AOCD	%	No.	Thalassemia %
OPD	27		44.3	8		28.6	9	81.8
IPD	34		55.7	20		71.4	2	18.2
Total	61		100	28		100	11	100

Discussion

The pathogenesis is well-defined, and a systematic approach to arriving at a clear diagnosis of microcytic hypochromic anaemia has been established. Similar to our analysis, the most common causes of microcytic hypochromic anaemia in the majority of series were IDA and thalassemia trait [6]. Chronic illness anaemia is the second most common cause of anaemia after iron deficiency anaemia. In AOCD, the peripheral blood film is generally normocytic. The advanced condition causes red cells to appear microcytic and hypochromic. Other less frequent diagnoses that must be considered are including sideroblastic anemia, chronic lead poisoning, and X- linked sideroblastic anemia [7]. In this study out of a total of 100 patients of microcytic hypochromic Anemia, 61% patients had iron deficiency anemia, 28 % patients had anemia of chronic disease anemia and 11% patients had thalassemia. Iron deficiency is the most frequent haematological disorder, and iron deficiency anaemia is the most common cause of anaemia worldwide [8]. Although blood loss is a major cause of iron deficiency anaemia, dietary iron insufficiency remains the most common cause of iron deficiency anaemia in developing countries [9]. Iron deficiency can occur as a result of an iron-deficient diet, such as that followed by dedicated vegans [10]. Comparable to this study Patel et al. selected 100 anaemic patients from Shree Krishna hospital in GUJARAT in 2009 after obtaining a complete history and clinical evaluation [11]. They discovered 40 patients with iron deficiency anaemia in their investigation. Females were more affected than males. There were two peaks in age groups of 21-30 years and 31-50years, and the majority of patients (53%) were found to have moderate iron deficiency. Kaur & Kaur discovered that 98% of female respondents and 56% of male subjects were anaemic in a recent study done in the rural population of Patiala, one of Punjab's major cities [12]. It was also suggested that women's poor nutritional profiles are positively associated with haemoglobin levels. The distribution of iron deficiency anaemia (IDA) across age groups was investigated in this study. IDA predominates in the elderly 61-70 years (32.7%) followed by reproductive age 21-30 years (21.3%) followed by 18% of cases in the age group of 51-60 year. This study found that female patients had a higher prevalence of microcytic hypochromic anaemia (39% were male and 61% were female), and females were more prevalent across all age categories. In this study, iron deficiency anaemia was found in more females (65.6%) than men (34.4%), chronic disease anaemia was found in 57% of males and 42.9% of females, and thalassemia was found in 18.2% of males and 81.8% of females. The majority of studies have discovered that patients with iron deficiency anaemia typically have substantial gastrointestinal lesions, especially those of the upper gastrointestinal tract. Cook et al. discovered 40% of patients had upper gastrointestinal tract lesions, while Kepczyk et al. discovered 55% of patients had upper gastrointestinal tract lesions [13,14]. Upper gastrointestinal lesions were seen in 21.3% (13 of 61 iron deficiency anaemia patients) of our study participants. Upper gastrointestinal bleeds were caused by antral gastritis in 13.7% of cases, a duodenal ulcer in 10.3%, gastroesophageal varices in 6.8% of cases, and sliding hiatus hernia with gastritis in 3.4% of cases. The rate of lower gastrointestinal tract abnormality in iron deficiency anemia patients was 13.5-30%. In these studies, the most common lower gastrointestinal lesion was found to be hemorrhoid (28.7%) [15,16]. In our study, haemorrhoids were the most prevalent lower gastrointestinal lesion detected in 85.7% of iron

deficiency anaemia patients, which was slightly higher than in the previous study. Other lower gastrointestinal pathology includes inflammatory bowel disease-ulcerative colitis (4.7%), colonic diverticula (4.7%), and colonic cancer (4.7%). Menorrhagia was the major cause of iron deficiency anaemia in females of reproductive age [17].

In this study, we observed that in patients with iron deficiency anemia, a total of 11 female patients have menorrhagia (18%), out of these the most com- mon cause was dysfunctional uterine bleeding in 6 patients (54.5%) followed by uterine fibroid in 2 patients (18.1%) and other causes include uterine polyp, hypothyroidism, and carcinoma cervix.

According to J.B.Sharma et al amebiasis and giardiasis are common, and increased iron loss from hookworm infestations, schistosomiasis, chronic malaria, excessive sweating, and blood loss from the stomach due to haemorrhoids are also major causes of anaemia in pregnancy [18].

In our study 3 patients (16.6%) had hookworm infestation and 1 patient (5.5%) had Ascaris lumbricoides infestation. All these studies closely correlate with our study where iron deficiency anemia is more common in females (66.5%) than in males (34.4%), in females, the common age group were reproductive and post- menopausal age group 51-60 years, while in the male the common age group was elderly. The 2nd most common cause of microcytic hypochromic anemia is anemia of chronic disease (28%). The anemia of chronic disease/inflammation was more common in hospitalized patients. Out of the total patients with anemia of chronic disease, 28.6% were from OPD and 71.4% were from IPD. ACD has been observed in a number of situations, including severe trauma, diabetes mellitus, and geriatric anaemia, in addition to infections, inflammation, and cancer [19]. Chronic disease anaemia is still underdiagnosed and undertreated [20].

A recent research of 191 consecutive hospitalised elderly adults with anaemia discovered that 70% of patients had anaemia or chronic illness. Chronic renal failure was seen in 16% of patients with chronic anaemia. 71% of patients with chronic anaemia had an acute infection, 12% had malignancy, and 16% had a chronic infection, such as a pressure ulcer or a chronic autoimmune inflammatory illness [21]. In our study we observed that out of a total of 28 AOCD patients the most com- mon cause was an infection - Tuberculosis in 11 patients (39.2%) followed by chronic kidney disease in 3 patients (10.7%), followed by systemic lupus erythematosus in 3 patients (10.7%), next includes 2 patients from each of rheumatoid arthritis, multiple myeloma, diabetes mellitus, and other causes includes non-Hodgkin lymphoma, Hodgkin lymphoma, Chronic lymphocytic leukemia, carcinoma lung, and Crohn disease.

In the elderly, around 10322% of anaemia is thought to be attributable to inflammation, as circulating IL-6 levels rise with age, though there are numerous other causes of anaemia that become more common with age, including iron efficiency and other diseases [22].

Chronic illness anaemia has been classified according to age groups. Following distribution, it is clear that the majority of patients suffering from chronic anaemia are between the ages of 41 and 70.

Anemia is common in tuberculosis patients, and it may be more prevalent in individuals who are infected with both TB and HIV [23]. More over three-quarters (77%) of TB patients without HIV were anaemic in one Malawi research, while 88% of TB/HIV infected patients were anaemic [24]. Dr. Sunanda Mondal et al. examined Microcytic Hypochromic Anemia and categorised 150 cases into three groups: Group-1 (iron deficiency anemia-IDA) cases 90 (60%), Group-2 (anaemia on chronic disease-ACD) cases 31 (21%), and Group-3 thalassemia cases 29 (19%). Iron deficiency anaemia (IDA) was found to be more common (84%) in reproductive-age females (31-40 years) than in pre or postmenopausal women (41-50 yrs.). The bulk of ACD instances discovered in Group 2 were in the elderly, who were suffering from various types of chronic illness. These age groups are primarily above 50, with men outnumbering women (74%) [25].

The finding and distribution of iron deficiency and AOCD in our study closely correlate to the above study.

Thalassemia (11% of the cases) is the third cause of microcytic hypochromic anaemia. In the Indian subcontinent, thalassemia is a common hereditary illness. Because severe alpha-deletion mutations are less common in this region, alpha-thalassemia is not a major issue in India. The carrier rate for -thalassemia ranges between 3 and 17%. In India, the percentage of thalassemia carriers ranges from 1 to 80 percent. However, it is less clinically relevant than β-thalassemia [26].

In our study, we observed that out of a total of 11 thalassemia patients most common were b-thalassemia traits in 81.8 %, followed by 9% of each Delta B – thalassemia and double heterozygous HBE and B thalassemia. Of these patients 18.2 % were males and 81.8% were females. The difference in the sex distribution is might be due to different age groups. In our study, we included the adult population mostly.

Conclusion

Anemia is not an illness in and of itself, but rather a symptom of another, hence finding the under- lying

cause is significantly more important. This study was undertaken to analyse the aetiologies of microcytic hypochromic anaemia, and it found that iron deficiency anaemia (IDA) is the most common cause, followed by chronic illness anaemia and thalassemia. All patients with Microcytic hypochromic anaemia should have a complete evaluation, including a hemogram and a peripheral blood film. Before iron supplementation, a serum iron profile, bone marrow iron stain, and haemoglobin electrophoresis must be performed to confirm the aetiology. People suffering from chronic illnesses, which form a large group as a result of nutritional insufficiency and anaemia from chronic diseases, can be avoided to some extent by the ongoing and uninterrupted implementation of anti-tuberculosis programmes in third-world countries such as India. Carrier screening programmes have been helpful in raising awareness of thalassemia among the general public in thalassemia-prevalent developing countries. Although precise data on thalassemia prevalence in our country is not accessible. We discovered a significant number of patients with thalassemia characteristics in this investigation. To lessen the burden of thalassemia, mass awareness, premarital counselling, and prenatal diagnostics should be implemented.

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