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Original Research Article

Study on Incidence of Pathologies/Chronic Illnesses, Morphological Patterns and TheirAssociations in Anemia of Chronic Disease

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Abstract:

Background and Objectives: Anemia of chronic disease (ACD) is the second most prevalentanemia overall after iron deficiency anemia which develops under the setting of chronic infections, cancer or autoimmune diseases. Detection of the type of anemia is important to execute a correct treatment plan. Identification of anemia of chronic disease will definitely have great impact on treatment. To study the incidence of morphological patterns in anemia of chronic disease. To evaluate the incidence of chronic illnesses manifesting as anemia of chronicdisease. To evaluate the frequency of association of morphological patterns with diseaseentity

Methodology: 100 cases of age group between 18-80 years having chronic illnesses attending the outpatient clinic as well as admitted patients of JNKTMCH, Madhepura. with hemoglobin <13 g/dl (haematocrit <39%) in men andwomen with hemoglobin <12g/dl (haematocrit <36%) included in the study. The hematological parameters were analyzed using automated hematology analyzer Mindray BC-3000 plus. The morphological patterns of the red blood cells were studied in peripheral smears. Anemia of chronic disease was identified using Serum ferritin assay, serum iron estimation and total iron binding capacity.

Conclusion: ACD is an unrecognized problem and diagnosis of ACD is the need of an hour. Thus, the present study was undertaken, keeping this need in view.

Keywords: Anemia of Chronic Disease; Incidence; Morphological Patterns;Frequency.

Introduction

Anemia is the most common haematological disorder, a global problem of immense health significance. Anemia of chronic disease (ACD) is the second most prevalent form of anemia after iron deficiency anemia (IDA). [1] Anemia of chronic disease(ACD) is a hypo proliferative anemia occurring in chronic infectious, inflammatory or neoplastic disorders. This form of anemia is an adverse consequence of systemic illness that is not due to bleeding or hemolysis. [2,3] ACD does not include the anemia's caused by endocrine, renal, or hepatic insufficiency. [2] ACD is characterized by mild (> 100 g/L) or moderate (85–100 g/L) reductionsin hemoglobin concentrations. In a minority of patients, severe reductions can occur. This mild to moderate normocytic to microcytic anemia is found with a frequency between 8% and 95%. [4,5,6] The estimated prevalence of anemia of chronic disease causeddue to chronic inflammation accounts to 23-50%. The condition has thus been termed as "anemia of inflammation". [7] ACD in chronically ill patients has a negative impact on quality of life as well as survival, the ability to diagnose this disorder depends on the ability of the physician to correlate the possible clinical pathways of underlying disease with patients ferrokinetic state. [8] The cytokines and acute phase proteins play an important role in pathogenesis of ACD. Hepcidin molecule has the ability to reduce the function of ferroportin on duodenal enterocytes, macrophages, placental cells and hepatocyte, which leads to impaired iron absorption from the gut and exaggerated iron retention, which is a hallmark of anemia of chronic disease. [4] Misdiagnosis with IDA has to be ruled out as thismight lead to refractoriness to standard therapy. The present study was undertaken to highlight the incidence of chronic illnesses, morphological patterns and association thereof in anemia of chronic disease, to establish anemia in chronic diseases using lab parameters like serum ferritin, serum iron, total ironbinding capacity. ACD is quite often neglected or improperly treated. Detection of the type of anemia is important to execute a correct treatment plan. Anemia of chronic disease is quite distinct due to the fact that it is not as a result of deficiency but due to factors impeding the availability of iron, inflammation is one such impeding factor causing anemia of chronic disease. Mere removal or reduction of inflammation inflammation may not correct

the anemic status. It has to be supported with appropriate therapy.

The study focuses on aspects like incidence, morphological pattern and their frequency of association in anemia of chronic disease, a correct identification of anemia of chronic disease will definitely have great impact on treatment. Hepcidin has emerged as one such molecule which has caught the attention of researchers. Hepcidin antagonist has now emerged as critical drugs which would modify the disease course in chronic illnesses. Further evaluation of this acute phase protein along with other hematologic parameters will throw some light on this common yet intriguing disease called anemia of chronic disease.

Objectives

To study the incidence of morphological patterns in anemia of chronic disease.

To evaluate the incidence of chronic illnesses manifesting as anemia of chronic disease. To evaluate the frequency of association of morphological patterns with diseaseentity.

Material and Methods

100 cases of age group between 18-80 years having chronic illnesses attending the outpatient clinic as well as admitted patients of JNKTMCH, Madhepura. with hemoglobin <13 g/dl (haematocrit <39%) in men and women with hemoglobin <12g/dl (haematocrit <36%) included in the study. The hematological parameters were analyzed using automated hematology analyzer Mindray BC-3000 plus. The morphological patterns of the red blood cells were studied in peripheral smears. Anemia of chronic disease was identified using Serum ferritin assay, serum iron estimation and total iron binding capacity.

Inclusion Criteria

- Patient having chronic illnesses.
- Patient within age group range 18-80yrs
- Men with haemoglobin <13g/dl (haematocrit <39%) and women withhaemoglobin <12g/dl (haematocrit <36%).

Exclusion Criteria

- Previously diagnosed cases of thalassemia / sideroblastic anemia/lead poisoning/ iron deficiency anemia.
- Patients aged less than 18years.
- Patients with Congenital anemia's.
- Women bearing children (pregnancies)
- Patients with acute blood loss.

Blood samples were collected aseptically in EDTA and Plain vacutainers. EDTA vacutainers for hematological investigations. Plain vacutainers was used for serum ferritin, serum iron and TIBC. Serum was separated and taken for Serum Ferritin Assay, serum iron estimation and total iron binding capacity. As a part of complete blood count, Hb %, Packed cell volume(PCV), RBC count, RBC Indices (MCV, MCH, MCHC), Red cell distribution width (RDW), White Blood Cell Count & Platelet Count was analyzed using auto hematology analyzer mindray BC-3000 plus. Serum ferritin assay, Serum iron estimation and total iron binding capacity were done by biochemical methods. Serum ferritin was done using enzyme linked flororosense immune assay, and serum iron and TIBC was done using spectrophotometric method.

Serum iron

Procedure

	Blank	**Standard**	**Sample**
Reagent	1000µL	1000 µL	1000Ml
Distilled Water	40µL	-	-
Standard	-	40 µL	-
Sample	-		40µL

TIBC determination

	Blank	**Standard**	**Sample**
Iron Reagent	1000µL	1000µL	1000µL
Distilled Water	40µL	-	-
Iron Standard		40 µL	-
TIBC Supernatant	-	-	40µL

Results

In the present study we found out the incidence of chronic illnesses causing ACD, morphological patterns and association thereof in anemia of chronic disease on 100 cases which satisfied the inclusion & exclusion criteria as per our study methodology. The results and observation of the study were summarized below.

The following table represents the division of patients according to their age group.

Table 1: Distribution of study subjects according to theirage

S No.	Age Distribution	Number of Patients	Percentage (%)
1	21-30 Years	7	7 %
2	31-40 Years	14	14 %
3	41-50 Years	22	22 %
4	51-60 Years	32	32 %
5	61-70 Years	15	15 %
6	71-80 Years	10	10 %
	Total	**100**	**100 %**

Table 2: Gender distribution of the study subjects

S No.	Gender	No. of Patients	Percentage (%)
1	Male	66	66%
2	Female	34	34%

100 cases 66(66%) were females. Male: Female ratiowas found to be 1.94:1. According to the above pie diagram of gender wise distribution of cases. Themajor bulk of the study population is formed by male gender.

Table 3: RBC counts in the patients with anemia of chronicdisease

S No.	Sex	RBC Count	No. of Patients	Percentage (%)
1	MALE	< 4.5 X 10^6/Microlit	65	65 %
2		4.5 – 5.5 X 10^6/Microlit	1	1 %
3	FEMALE	< 4 X 10^6/Microlit	34	34 %
4		4 – 5 X 10^6/Microlit	0	0 %

In the present study of 100 cases, RBC count was decreased in65% of males and 34% in females, and it was normal in 1%.

Table 4: Packed cell volume values in the study population

S No.	Packed Cell Volume	No. of Patients	Percentage (%)
1	< 37 %	99	99 %
2	37 – 47 %	1	1 %
3	> 47 %	0	0 %

Out of 100 cases of study population, MCV was normal in 78cases (78%), it was decreased i.e. less than 80 f L in 22 cases (22%). This graph depicts majority of the cases were between 80-100fL.in 100 ACD cases, there were 37 tuberculosis cases, 20 cases (54%) had normocytic normochromic pattern, 11 (29.7%) had microcytic hypochromic pattern and 6 cases (16%) had normocytic hypochromic pattern.

Out of 23 cases of rheumatoid arthritis, 12 cases (52.17%) had normocytic normochromic pattern, 6 cases (26.08%) had normocytic hypochromic pattern and 5 cases (21.74%) had microcytic hypochromic pattern. 12 cases of HIV were present, 9(75%) had normocytic normochromic pattern, 2(16.66%) had normocytic hypochromic pattern and 1 (8.33%) had microcytic hypochromic pattern.

In 8 Malignancy (Ca Breast) cases, 6(75%) had normocytic normochromic pattern and 2 cases (25 %) had microcytic hypochromic pattern.

7 COPD cases had 6 cases (85.7%) having normocytic normochromic pattern, 1(14.28%) had normocytic hypochromic pattern. In 7 SLE cases, 5 (71.43%) had normocytic normochromic pattern, 1(14.28%) had normocytic hypochromic pattern and 1(14.28%) had microcytic hypochromic pattern. Out of 4 Hodkins lymphoma cases, 3 (75%) had normocytic normochromicpattern and 1 (25%) had microcytic hypochromic pattern & in 1 Non Hodkins lymphomacases, 1 (100%) had normocytic normochromic pattern.

Discussion

ACD is the second most prevalent anemia only after iron deficiency. Unfortunately, it is commonly under diagnosed in clinical practice, and is frequently misunderstood and managed inappropriately. ACD still remains a bag of unsolved questions in terms of treatment. Significant gaps remain in comprehension of the true incidence of diseases leading to ACD and consequences of ACD. The present study was to establish the incidence of chronic illnesses causing anemia of chronic diseases, the morphological pattern of anemia in ACD, and the frequency of morphological patterns with the chronic illness in ACD. Once the clinical diagnosis was established based on clinical signs and symptoms. The laboratory features were resorted for. Diagnosis of ACD began with hemoglobin estimation, pattern manifest in peripheral smear and the erythrocyte indices for correlation, we had taken into account the parameters MCV and Peripheral smear findings for the initial workup in cases with reduced hemoglobin. When pattern was normocytic, a reticulocyte count was considered. A low reticulocyte count prompted evaluation of

WBC and platelet parameters which when at their lower limits bone marrow failure would be the case. We had normal to high counts which prompted us to consider the diagnosis of ACD. Serum iron, Serum ferritin, TIBC were performed in these cases. All the cases had normal to increased serum ferritin, normal to decreased TIBC, and decreased serum iron. With the microcytic pattern a normal and high serum ferritin level prompted evaluation of serum iron level and TIBC, a decreased serum iron level and decreased and normal TIBC suggested ACD. Whereas IDA was ruled outwhich will have serum iron level decreased with increased TIBC. Sideroblastic anemia, thalassemia and others were ruled out which would have normal iron level.

Table 5 : Distribution of erythrocyte indices in acd

	Wians Jr FH *et al*[8]	Present Study
MCV	87.5 ±7.8	83.97±6.05
MCH	29.5±2.9	27.09±1.76
MCHC	33.7±0.7	30.88±2.3

Normal MCV being 80fl-100fl. In the present study the MCV was in the range of 83.97±6.051 which was concordant with the study conducted by Wians Jr FH *et al* with MCV range of 87.5 ±7.8. Majority of the cases in our study had normal MCV suggesting that ACD was of recent onset whereas few cases with low MCV pointed out the ACD existed over a long period of time. In the present study mean MCV was 83.9, Cash *et al* [9] concluded in a study conducted on 90 patients of ACD that mean red cell volume was 86 fl. MCV is a good indicator of ACD when in normal range, when reduced the other studies like peripheral smear, RDW, serum ferritin, TIBC, serum Iron has to be considered to rule out other cause of anemia.

In the present study the mean MCH was 27.09 and was in the range of 27.09±1.76 which was concordant with the study conducted by Wians Jr FH *et al* with hemoglobin range of 29.5±2.9. In the present study the mean MCHC was 30.88 with a range of 30.88±2.3 which was concordant with the study conducted by Wians Jr FH *et al* with MCHC range of 33.7±0.7 This was different from the study conducted by s Giannouli S *et al* [10], who had normocytic hypochromic anemia as the predominant type.

In the present study we had 4 Hodkins lymphoma cases, 3 (75%) had normocytic normochromic pattern and 1 (25%)had microcytic hypochromic pattern which showed concordance with the study conducted by Hohaus S *et al* out of 65 patients of hodkins lymphoma, anemia was normocytic normochromic in 19 patients, while it was microcytic in 8 patients. In the present study we had one Non-hogkins lymphoma and one case of Osteomyelitis which had Normocytic Normochromic pattern (100%). Out of 12 HIV cases in this study, 9(75%) had normocytic normochromic pattern, 2(16.66%) had normocytic hypochromic pattern and 1 (8.33%) had microcytic hypochromic pattern. Kotwal J *et al* [11] studied 55 HIV infected symptomatic patient. Anemia was present in 45 patients and out of which 66.66% patients had normocytic normochromic anaemia. Iron deficiency anaemia was present in 37.77% patients and anaemia of chronic disease in 62.22% patients. 2 patients had anaemia of the critically ill. Kreuzer KA *et al*[12]quoted microcytosis is rarely observed in HIV infection, whilenormocytosis appears to be commonly found in these patients. Out of 8 Malignant cases (Ca Breast), 6(75%) had normocytic normochromic pattern and 2 cases (25 %) had microcytic hypochromic pattern. Cash JM *et al* [9] quoted Cancer is the cause of anemia in 19% of cases of ACD with normocytic normochromic anemia being the most common pattern.

Conclusion

One of the most important areas for scope in the improvement of health care is prevention of anemia. Anemia of chronic disease is the 2nd most common anemia worldwide and the most common anemia in elderly. Anemia of chronic disease is known to be associated with mortality in many disorders. Hence timely diagnosis and effective management is important. Adults being the most vulnerable group for anemia of chronic disease, they require early screening and subsequent diagnosis for appropriate management.

In the present study, age group of 18-80 yrs were studied, and 5th decade were found to be most affected with male preponderance. Most common morphological pattern was normocytic normochromic, followed by microcytic hypochromic and normocytic hypochromic anemia. Tuberculosis was the most common cause leading to anemia of chronic disease followed by rheumatoid arthritis and others.

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