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ASSOCIATION OF ANEMIA IN RHEUMATOID ARTHRITIS WITH THE SEVERITY OF DISEASE ACTIVITY

General Medicine

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is an autoimmune disease, in which anemia is commonly encountered. The present study was done to assess the clinical presentation of patients diagnosed with RA in our department to assess the prevalence of anemia in these patients. **Methodology:** This observational cross-sectional study included patients diagnosed with RA according to the American Rheumatologic association criteria 1987, from the age group 20 to 60 years with disease duration of disease up to 5 years. Anemia was defined as a haemoglobin level < 13 g/dl in men and < 12 g/dl in women. **Results:** During the study period, 100 RA patients were included, 73% had anemiaOf these, 39% had anemia of chronic disease (ACD), 23% had iron deficiency anemia (IDA), 6% combined IDA+ACD and 5% had megaloblastic anemia. The median duration of disease was similar in patients with or without anemia (3.76 years vs 2.87 years, p value = 0.45). Median swelling joint count was significantly higher in those with anemia as compared to those without anemia (14 vs 6, p value <0.05). Median tender joint count was similar (Table 3). We also observed that median ESR, CRP and median DAS score was significantly higher in patients with anemia. We found that 92% of the patients with anemia were positive for rheumatoid factor, while 81.5% of those without anemia had rheumatoid factor. **Conclusions:** ACD was the most common type of anemia. Presence of anaemia may serve as predictor of disease activity in RA patients.

KEYWORDS

anemia; disease activity; rheumatoid arthritis; severity

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease with a worldwide prevalence of approximately 0.5% to 1% among adults.[1] When RA is left uncontrolled, the RA patient may experience joint deterioration, severe disability, decreased quality of life, the onset of comorbidities and premature mortality.[2] Anaemia is a common characteristic of RA. Garrod first noted the association of RA with anaemia.[3] Prevalence of anaemia in RA ranges from 30-70% in different studies.[4] Overall anaemia of chronic disease and iron deficiency anaemia are frequent causes of anaemia in RA patients,[5] but in developing countries like India, nutritional deficiency may also be a major associated problem adding to the etiology in genesis of anaemia in RA patients. The influence of anaemia on the RA disease course could be significant Borah and colleagues in a study in Northern India found a prevalence of 64 % among patients who had been on follow up with RA for a period of more than 2 years and in this cohort, 65% of the anaemia observed was anaemia of chronic disease (ACD) while iron deficiency anaemia (IDA) accounted for 33% the anaemia. The ACD and IDA, alone or in combination are the most frequent forms of anaemia in RA. Changes in iron metabolism cause anaemia of chronic disease in RA patients and are mainly induced by the altered synthesis and function of hepcidin and ferroportin, which are induced by pro-inflammatory cytokines, mainly IL-6.[6] The present study was done to assess the clinical presentation of patients diagnosed with RA in our department to assess the prevalence of anemia in these patients.

METHODOLOGY

Study Design and Sample population

This observational cross-sectional study included patients diagnosed with RA according to the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR), 2010[7], from the age group 20 to 60 years with disease duration of disease up to 5 years. We excluded patients with previously diagnosed anemia and treated for it, with history of bleeding disorder not related to RA, with mixed disorder like SLE and RA; SS& RA and MCTD and overlap syndrome and those with previously known malignancies, renal failure, hemolytic anemia any other chronic blood loss like hemorrhoids. Patients were enrolled from the Rheumatology clinic, Department of Medicine, DY Patil School of Medicine, Navi Mumbai from March 2018 till August 2019. The patients were explained the purpose of the study and an informed written consent was obtained from them. The study was approved by the Institutional Ethics Committee.

Data Collection and Data Analysis

Using a pre-designed semi-structured study proforma, we noted the patient related information. Demographic details included gender, age at onset and duration of disease. Disease characteristics recorded for all patients included 28-swollen joint count, 28-tender joint count, duration of early morning stiffness in minutes. The selected patients were evaluated with detailed history regarding duration of disease and history of drug intake and type of onset of symptoms noted. Presence of joint swelling, tenderness and deformities and number of tender joints and number of joint swelling noted. Detailed clinical examination including all systems were examined and visual analogue pain score was assessed. Severity of disease activity was measured using the Disease Activity Score (DAS), which is a score is a composite score using tender and swollen joints count, ESR and patients global assessment activity using a 100 mm visual analogue scale. Using this scale, patients were classified as mild <3.1, moderate 3.2-5.1 and severe >5.1 (minimum score :0; maximum score : 9). For using DAS, parameters included were: total 28 joint count for tenderness, total 28 joint for swelling, Erythrocyte Sedimentation Rate (ESR) in mm in first hour and patient assessment of global health using a 100mm visual analogue scale ranging from 0 (very good) to 100 (very poor). All patients underwent x-rays of extremities as determined by the treating physician. Laboratory investigations included complete blood count, ESR, C-reactive protein (CRP), rheumatoid factor, Anti-cyclic citrullinated peptides (anti-CCP) autoantibodies. Anemia was defined as a haemoglobin level < 13 g/dl in men and < 12 g/dl in women.

Data were coded and recorded in MS Excel spreadsheet program. SPSS version 23 was used for data analysis. Descriptive statistics were described using means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Group comparisons were made using independent sample t-test for continuously distributed data, and chi-squared test for categorical data. Appropriate non-parametric tests (Wilcoxon test/Kruskal Wallis Test/Spearman Correlation) were used when the data were non-normally distributed. Level of significance was taken as $p < 0.05$.

RESULTS

During the study period, 100 patients diagnosed with RA were included. The mean age was 46.4 years ranging from 22 to 60 years. The most common age group was 41 to 60 years (Table 1). Females comprised 75% of the patients. It was observed that 47% of the patients had moderate disease activity, 26% had high disease activity, 25% had low disease activity and only 2% of the patients were in remission. Rheumatoid factor was found to be positive in 89% of the patients and high anti-CCP antibodies were found in 97% of the patients. The most common presenting symptoms were a combination of pain, swelling and deformity, which was observed in 47% of the cases (Table 2). Common joints involved were wrist joint (75%), proximal interphalangeal joint (66%) and metacarpophalangeal joint (66%). The common joint deformities were wind swept deformity (20%) and swan neck deformity (18%). Other less common joint deformities were fixed flexion deformity, Z deformity, hallux valgus, plantar subluxation of metatarsal heads and Boutannier deformity. We observed that 73% of the patients developed anemia. It was determined

that 39% of the patients had anemia of chronic disease (ACD), 23% had iron deficiency anemia (IDA), 6% combined IDA+ACD and 5% had megaloblastic anemia.

The median duration of disease was similar in patients with or without anemia (3.76 years vs 2.87 years, p value = 0.45). Median swelling joint count was significantly higher in those with anemia as compared to those without anemia (14 vs 6, p value <0.05). Median tender joint count was similar (Table 3). We also observed that median ESR, CRP and median DAS score was significantly higher in patients with anemia. We found that 92% of the patients with anemia were positive for rheumatoid factor, while 81.5% of those without anemia had rheumatoid factor.

DISCUSSION

Anemia is not considered a major problem in RA by the vast majority of physicians. We observed that 73% of the patients developed anemia. The most common type was ACD. In a similar study by Goyal et al, 55% of the anemics in their study were diagnosed with ACD, while IDA was observed in 27.5% of the patients.[8] Similar results were demonstrated Agrawal in which ACD was seen in 51.6% and IDA in 48.4% anemic RA cases.[9] In the study by Adriana Sabauet et al 70.4.% patients were anaemic in which IDA was present in 47.36% patients and the rest of 52.63% patients had ACD.[10] In various other cross-sectional studies, ACD has been reported to be present in 30% to 70% of patients with RA.[11] In the study by Yadav et al, the prevalence of anaemia was 33% in the study population. 24.7% of the patients in the study population had ACD while 8.3% had IDA.[12]

We also found that those with anemia had significantly higher median swelling joint count, higher ESR, CRP, and median DAS. However, the presence of anemia was not significantly associated with the duration of disease, tender joint count and the presence of rheumatoid factor. Goyal and colleagues reported that the patients with anemia had higher levels of mean DAS28 score and ESR, which is similar to the results of the present study. In addition, Goyal et al found that these patients had more joints involvement and higher pain score. Since both ESR and DAS28 depict the severity of disease activity, presence of anemia also indicates active disease. ESR is a marker of chronic inflammation and anemia could be the result of inflammation. So raised ESR is significantly related to the presence of anemia. In a recent study by Yadav et al, there was a statistically significant increased chance of being anaemic as the disease activity score increased from remission to high disease activity (p<0.001), as out of 66 patients with anaemia 45 (68.3%) patients had high disease activity. Kumari et al also reported that anemic patients also had significantly higher number of tender joints (p=0.025) and swollen joints (p=0.043) which reflects that severity of anemia is related with disease activity and inflammation.[13]

We did not observe a significant association between the presence of anemia and RF positivity. Similar to our findings, Goyal et al reported that RF positivity was found in 80% anaemic RA patients and in 63.15% non-anaemic patients, and the association between RF and anaemia was not statistically significant (p>0.05). The authors explained this finding by the relatively small sample size of the study, which may be the case in our study as well. This is further supported by the fact that a study with a large sample size like the ERAS inception cohort, anaemic patients experienced a more aggressive course of joint destruction.[14]

CONCLUSION

Based on the results of the present study, it can be suggested that anaemia may serve as predictor of disease activity in RA patients. Diagnosis of anemia in RA should encourage the treating physician to thoroughly investigate the patient for disease activity and periodic assessment of hemoglobin levels.

Table 1. Baseline characteristics of the patients included in the study

Variables	Frequency	Percent
Age group (years)		
Up to 40	44	44%
41 to 60	56	56%
Gender		
Male	25	25%
Female	75	75%
Disease activity		
High	26	26%
Moderate	47	47%
Low	25	25%
Remission	2	2%
Rheumatoid factor		
Positive	89	89%
Negative	11	11%
Anti-CCP		
>5 u/ml	97	97%
<5 u/ml	3	3%

Table 2. Presenting symptoms and joint examination of patients included in the study

Variables	Frequency	Percent
Presenting symptoms		
Pain	18	18%
Pain + Swelling	20	20%
Pain + Deformity	15	15%
Pain + Swelling + Deformity	47	47%
Joint involvement		
Proximal Interphalangeal Joint	66	66%
Metacarpophalangeal Joint	66	66%
Wrist Joint	75	75%
Elbow Join	33	33%
Shoulder Joint	17	17%
Knee Joint	38	38%
Ankle Joint	49	49%
Metatarsophalangeal Joint	12	12%
Joint deformity		
Wind swept deformity	20	20%
Swan neck deformity	18	18%
Fixed flexion deformity	13	13%
Z deformity	10	10%
hallux valgus	9	9%
plantar subluxation of metatarsal heads	10	10%
Boutannier deformity	8	8%

Table 3. Comparison of patient variables between anemic and non-anemic patients

	Anemia		p value
	Anemia (n=73)	No anemia (27)	
Duration of disease (years)	3.76	2.87	0.45
Swelling joint count	14	6	< 0.05
Tender joint count	7	11	0.67
ESR	54.6	30.63	< 0.05
CRP	14.5	5.99	< 0.05
DAS score	4.64	3.14	< 0.01
Rheumatoid factor present	92%	81.50%	0.61

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