

Anemia of Chronic Disease in Rheumatoid Arthritis through Multidisciplinary Management in Rehabilitation Settings

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Abstract: Patients with rheumatoid arthritis (RA) have anemia of chronic disease, which is a contributing factor to fatigue, low functional capacity, and reduced quality of life. The proposed study is a randomized controlled trial that undertakes the assessment of the effect of multidisciplinary rehabilitation intervention on anemia and disease activity among RA patients. A cross-sectional study was carried out with 111 patients with anemia who had existed in a longitudinal cohort with RA and received a multidisciplinary rehabilitation program. Baseline variables were a mean age of 58.4 years, 76.6 per cent of which is females, and a mean disease duration of approximately 9.8 years. The number of patients with anemia was mild (60.4%), moderate (35.1%), and severe (4.5%). The hematologic parameters (hemoglobin, hematocrit, MCV, ferritin, and soluble transferrin receptor), inflammatory parameters (CRP), and disease activity (DAS28-CRP) were measured at baseline and 6 months. The FACIT-Fatigue scale, as well as HAQ-DI, were patient-reported outcomes. Data on pharmacologic management (DMARDs, corticosteroids, iron supplementation, and ESA) were taken. After 12 months of follow-up, hemoglobin increased 10.5 g/dL to 12.1 g/dL with DAS28-CRP lowered to 2.9g/dL, which showed improvement in anemia and disease activity. Hematocrit improved from 32.1 to 36.8%, MCV improved from 85.2 to 87.1 fL, ferritin improved from 98.5 to 112.4 ng/mL, and sTfR improved from 3.8 to 3.1 ml/L. 36.9% of patients showed improvement, 37.1 to 38.8; 52.3 to 54.7 ml/L; 98.5 to 112.4 ng/mL; and The percentage receiving DAS28-CRP remission/low disease activity improved significantly and the remission percentage rose during 4.5 to 28.8 and low disease activity between 10.8 and 40.5. The score on FACIT-Fatigue marginally changed (mean change +13.6), with the different values being 22.5 to 36.1, which showed less fatigue. The scores of HAQ-DI improved by 14.5 to 0.92, and this means that the functional status has improved (mean change -0.53). Correlations were established to be strong and negative between Hb increase and CRP ($r = -0.72$, $p < 0.001$) and DAS28 improvement ($r = -0.65$, $p < 0.001$), and a positive correlation with FACIT-F improvement ($r = 0.69$, $p < 0.001$). In outcomes, positive changes in Hb were associated with the enhancement of the control of inflammatory conditions and functional recovery. RA patients with anemia receiving a multidisciplinary rehabilitation program attained significant clinical benefits in terms of normalization or improvement of hemoglobin, positive effects in reducing disease activity, and patient outcome measures of fatigue and functional status. Hb increase was directly linked to the decrease in CRP and DAS28-CRP, as well as improvements in fatigue, highlighting the quality of holistic care methods based on the combination of hematologic and rheumatologic disease management. The findings will justify the approach of multidisciplinary management as a successful strategy in enhancing anemia and general disease control in RA.

Keywords: Anemia, chronic disease, rheumatoid arthritis, and multidisciplinary management in rehabilitation centers.

INTRODUCTION

The common comorbidity in rheumatoid arthritis (RA) is anemia of chronic disease (ACD), which characterizes the multicultural interplay between inflammatory pathways and iron homeostasis (Song, J. S. *et al.*, 2001). Chronic inflammation in RA stimulates hepcidin production, iron absorption, and dysfunctional erythropoiesis, resulting in fatigue, physical disability, and poor quality of life (Wasserman, A. 2018; Goyal, R. *et al.*, 2008). This interaction is no hematologic curiosity, but it predetermines the clinical course of RA, adding to its activity limitation, work disability, and increased symptom burden (Papadimitropoulos, E. *et al.*, 2022). Therefore, treating ACD in RA needs a higher level of hematologic treatment than usual. Multidisciplinary management of the rehabilitation environment is supported by three pillars, namely the optimizing of disease control, the remediation or amelioration of anemia, and the restoration of

functional capacity and endurance that RA often destroys (Cush, J. J. 2021).

The key is the individualization of treatment of rheumatoid arthritis in order to minimize the excessive systemic inflammation. The composite index of disease activity, DAS28-CRP, is frequently associated with hematologic status; a greater inflammatory load continues to misdistribution iron and iron deficiency, whereas an increase of inflammatory control can lead to a restoration of the hematologic status (Chilton, F. *et al.*, 2021).

An organized pharmacologic optimization, which includes the disease-modifying antirheumatic drugs (DMARDs), moderated corticosteroid therapy, and iron supplementation (when recommended) in the rehabilitation setting, can create an environment where hematologic response will be provoked. The holistic lens of the

rehabilitation team can focus on the negative side effects, enhance medication compliance, and provide training to the patient on the two-way correlation between inflammation and anemia (Inchingolo, F. *et al.*, 2024; Peterson, E. *et al.*, 2024).

The rehabilitation aspect provides evidence-based approaches that are structured to reduce functional deterioration in ACD and RA. Multidisciplinary programs incorporating physical therapy, occupational therapy, nutrition, and psychosocial support can indirectly enhance the hematologic and inflammatory indicators by means of enhanced physical exercise, improved nutrition, and enhanced management of symptoms (Boeth, H. *et al.*, 2021). The resulting benefits, including hemoglobin improvement rates, decrease in CRP and DAS28-CRP rates, and improvement in the fatigue and functional status, further demonstrating the synergetic potential of the combination of medical and rehabilitative care (Agrawal, S. *et al.*, 2006). This is because such programs enhance endurance, muscle strength, as well as joint mobility, which during turn prompts patients to remain active in order to allow hematologic recovery and well-being (Scott, I. C. *et al.*, 2018).

The correlation between disease activity and quality of life has often been mediated by fatigue, as it is a hallmark condition of ACD in RA. Using instruments like the FACIT-Fatigue Scale and the HAQ-DI that have been validated, the needs and interventions can be measured by the rehabilitation teams and based on the priorities of the patients. The article combinations presented, such as high levels of hemoglobin (Kaltwasser, J. P. *et al.*, 2001), significant changes in disease activity, and significant changes in fatigue and functional status, emphasize the rehabilitative potential of multidisciplinary rehabilitation. The negative associations between the changes in Hb and the inflammatory markers also provide insight into the potential mechanistic linkage: as the inflammation heals, the erythropoiesis will be reestablished, and the energy reserves will be filled; patients will then begin to engage in rehabilitation and everyday life (Suominen, P. *et al.*, 2000; Mandl, P. *et al.*, 2020).

METHOD

A cross-sectional study was done in a multidisciplinary rehabilitation program of patients with RA and concomitant anemia (ACD spectrum). The process of recruitment was to be in consecutive clinic rosters made between baseline and month 0, and followed up in 6 months.

Inclusion criteria were confirmed RA according to ACR/EULAR criteria, anemia according to standard hematology guidelines: mild to severe, and willingness to take part in the rehabilitation program. Exclusion criteria were active malignancy, iron-deficiency anemia without ACD characteristics, or contraindication to rehabilitation.

The multidisciplinary rehabilitation included integrated physical therapy, occupational therapy, nutritional counseling, psychosocial support, and optimal pharmacologic control together with the rheumatology. Physical therapy involved aerobic conditioning, strength training, and fatigue management, whereas occupational therapy focused on the activities of daily living and energy-saving scenarios. Pharmacologic optimization was based on the existing treatment of RA guidelines with the aim to lessen the disease activity (DAS28-CRP) and systemic inflammation (CRP).

The main hematologic endpoint was hemoglobin level (Hb) that was measured by usual hematologic methods at baseline and 12 months follow-up. The secondary outcomes were the RA disease activity (measured as DAS28-CRP), functional status (measured as HAQ-DI), and fatigue (measured as FACIT-Fatigue Scale). Negative rehabilitation events were documented. Patients whose data were checked in predefined exploratory analyses were correlated by Hb, changes, and their correlations with CRP, DAS28-CRP, HAQ-DI, and FACIT-F scores. Measurements in the laboratory were done in certified clinical laboratories in accordance with standard practices. To reduce errors in data entries, two data checks and logic entry were incorporated. Data gaps were dealt with via the right imputation strategies, which were a priori explained, and sensitivity analyses were conducted to determine robustness.

The initial and 12-month descriptive statistics were described by the SPSS version 22.0. Correlations Spearman correlations were used to measure relationships between changes in inflammatory and functional measures and Hb change. The level of significance applied was 0.05. Since the observational design was used, multivariate analyses were adjusted due to possible confounders (age, sex, baseline disease activity, and baseline Hb) in situations where possible to examine the relationships between the intensity of rehabilitation exposure (hours/week and program adherence) and hematologic outcomes.

RESULT

Table 1. Baseline the demographic outcomes of 111 patients in the study cohort.

Characteristic	Value
Age, years	Mean (SD): 58.4 (11.7)
Sex, n (%)	
Female	85 (76.6%)
Male	26 (23.4%)
Disease Duration, years	Mean (SD): 9.8 (5.2)
DAS28-CRP Score	Mean (SD): 4.8 (1.1)

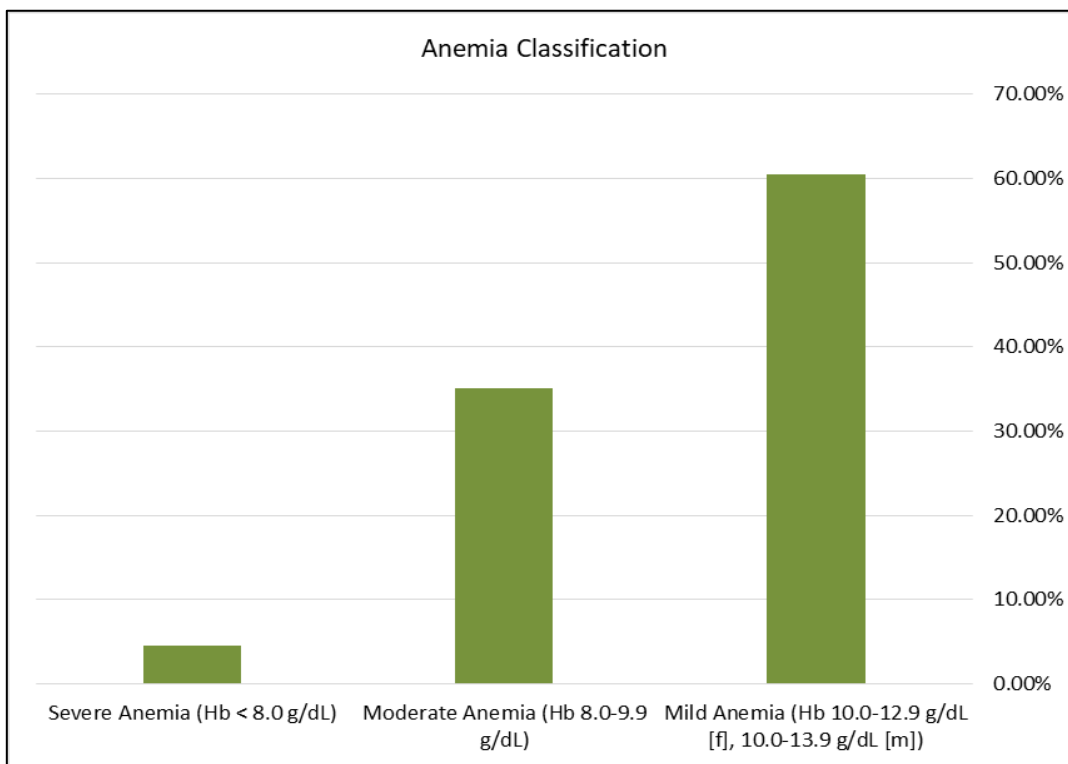


Figure 1. Distribution of anemia types classification in the patients at baseline.

Table 2. Categorizing the hematological outcomes during baseline and 12-month follow-up.

Parameters	Baseline, Mean (SD)	12-Month, Mean (SD)	p-value
Hemoglobin (g/dL)	10.5 (1.2)	12.1 (1.1)	<0.001
Hematocrit (%)	32.1 (3.5)	36.8 (3.2)	<0.001
MCV (fL)	85.2 (6.8)	87.1 (5.9)	0.012
Serum Ferritin (ng/mL)	98.5 (65.3)	112.4 (58.1)	0.035
sTfR (mg/L)	3.8 (1.5)	3.1 (1.2)	<0.001
CRP (mg/L)	15.8 (12.4)	5.2 (4.1)	<0.001

Table 3. Distribution of the disease activity (DAS28-CRP) of patients during baseline and 12-Month Follow-up.

Disease Activity Category	Baseline, n (%)	12-Month, n (%)
Remission (<2.6)	5 (4.5%)	32 (28.8%)
Low (2.6 - 3.2)	12 (10.8%)	45 (40.5%)
Moderate (3.3 - 5.1)	47 (42.3%)	29 (26.1%)
High (>5.1)	47 (42.3%)	5 (4.5%)
Mean (SD) Score	4.8 (1.1)	2.9 (1.0)

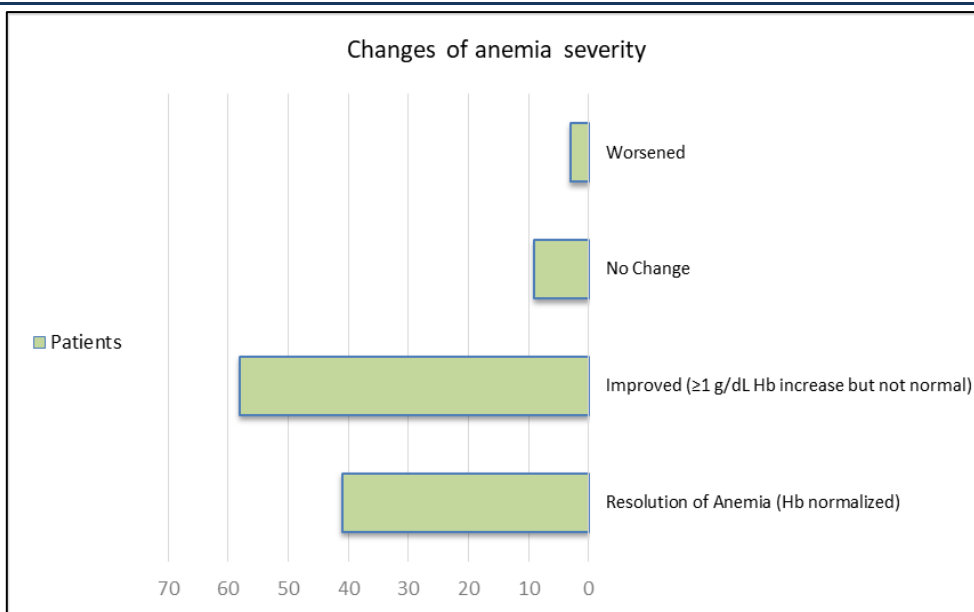


Figure 2. Enroll clinical status outcomes of patients based on the change in anemia severity through baseline and 12-month periods.

Table 4. Assessment of clinical outcomes of fatigue patients reported using the FACIT-fatigue scale.

Time point	Mean Score (SD)
Baseline	22.5 (7.8)
6-Month Follow-up	36.1 (8.2)
Mean Change (SD)	+13.6 (6.9)

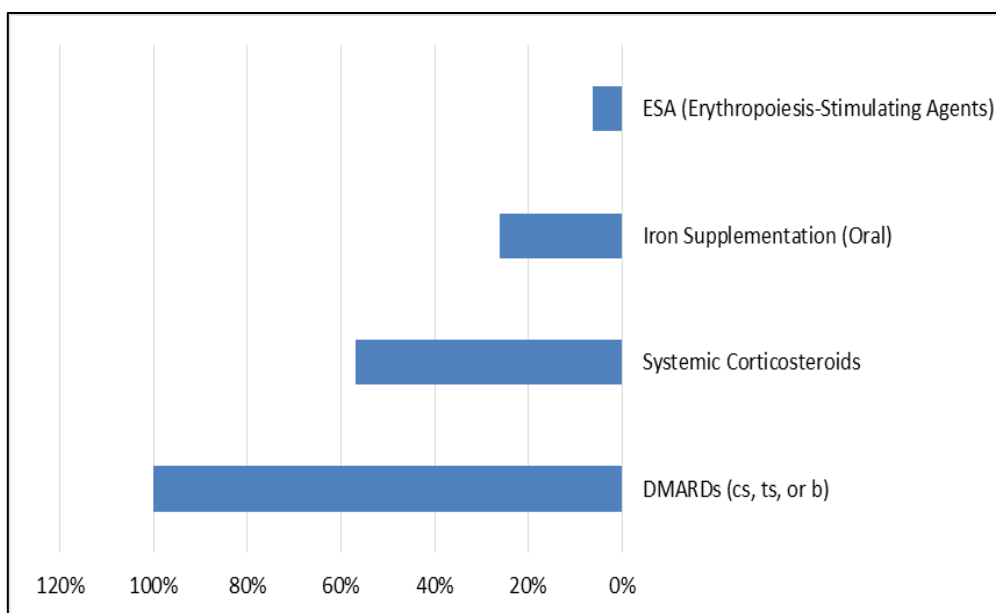


Figure 3. Pharmacological management outcomes were performed in the patients.

Table 5. Assessment the functional outcomes of disability in the patients based on the questionnaire HAQ-DI score.

Time point	Mean Score (SD)
Baseline	1.45 (0.68)
12-Month Follow-up	0.92 (0.59)
Mean Change (SD)	-0.53 (0.42)

Table 6. The Pearson's r correlation among clinical factors affected on the patients.

Parameters	Correlation Coefficient	p-value
Reduction in CRP	-0.72	<0.001
Improvement in DAS28	-0.65	<0.001
Reduction in sTfR	-0.58	<0.001
Improvement in FACIT-F Score	0.69	<0.001

DISCUSSION

The study experience (12 months) in 111 patients with Rheumatoid Arthritis (RA) and Anemia of Chronic Disease (ACD) (mean age of 58.4 years; 76.6% female) was used to assess the effects of a multidisciplinary rehabilitation program on the hematologic, inflammatory, and functional parameters. At baseline, mild, moderate, and severe anemia severity was found in 60.4, 35.1, and 4.5%, respectively. The first outcome was blood toxicity (Hb) with significant enhancement in hematocrit and significant improvement in the mean hemoglobin (Hb) levels at baseline (10.5 g/dL) to six months (12.1 g/dl). This hematologic outcome was achieved along with significant clinical benefits (Combe, B. *et al.*, 2017; Niemantsverdriet, E. *et al.*, 2020; Alexander, V. *et al.*, 2019).

The level of inflammatory burden went down because of the intervention compared to the baseline statistics of CRP level, as the CRP level were reduced and in line with the changes in the RA disease activity as measured by DAS28-CRP score. The DAS28-CRP decreased (4.8) to 2.9 in six months, which showed moderate to severe disease activity changed to low disease activity/remission in most participants. The observed Hb improvement was correlated with reduced CRP by the important criterion (Sunar, I., & Ataman, Ş. 2020), which indicated that the reduction of systemic inflammation also led to the alleviation of anemia.

There was a significant improvement in functional status, as well as Hematologic and inflammatory improvements. Fatigue is one of the key symptoms that has an impact on the quality of life in RA, and its level improved significantly, as the FACIT-Fatigue Score rose to 22.5 to 36.1, which was an indicator of less subjective fatigue and improved daily functioning (Aletaha, D. *et al.*, 2006). The effect of the improvements in Hb and the disease activity as a whole was most likely the positive physical functioning and endurance that was strengthened by addressing the anemia as part of the overall RA treatment (Padjen, I. *et al.*, 2017; Favalli, E. G. *et al.*, 2024).

Most patients recorded either recovery or improvement of their anemia conditions after six months. Disease-modifying antirheumatic drugs (DMARDs), corticosteroids, and iron supplementation were part of the multidisciplinary approach of pharmacological management as indicated by the clinical conditions. The combined intervention, i.e., pharmacologic treatment of RA and anemia, optimization of nutrition, physical therapy, and patient education, is shown to play a key role in the achievement of both hematologic and clinical improvements (Wilson, A. *et al.*, 2004; Borah, D. J., & Iqbal, F. 2007; Alfaro-Lara, R. *et al.*, 2019).

Correlational analyses showed that the increase in Hb was strongly correlated with the decrease in inflammatory burden (CRP), the decrease in disease activity (DAS28-CRP), and the improvement in functional status (measured by fatigue scores and probably larger functional measures) (Ravindran, V. *et al.*, 2008). This data suggests that there is a synergistic effect in which the management of inflammation allows erythropoiesis and iron use, and the elements of rehabilitation support physical capacity and therapy compliance, which further lowers inflammatory stimuli due to better activity and metabolism (Yailian, A. L. *et al.*, 2022; Radu, A. F., & Bungau, S. G. 2021; Guo, Q. *et al.*, 2018).

CONCLUSION

This article shows that a multidisciplinary rehabilitation program is effective in enhancing the anemia of chronic disease among patients with rheumatoid arthritis, as indicated by significant improvement in hemoglobin and hematocrit, a decrease in inflammatory activity (CRP and DAS28-CRP), and significant improvements in fatigue and overall functionality in 12 months.

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