

Iron profile and some hematological parameters among Sudanese patients with Rheumatoid Arthritis at Khartoum state

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Abstract:

Background Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by the involvement of numerous joints and by systemic symptoms, which leads to disability and premature death, Anemia is the most often hematological manifestation issue that occurs in RA.

Objective: This study aimed to evaluate CBC and to assess iron deficiency in RA Sudanese patients in Khartoum state.

Material and methods: This retrospective observational study was conducted on 63 RA patients and 63 healthy individuals as control between 2018 and 2021. The CBC and iron profile (serum ferritin, serum iron and total iron binding capacity) were carried out, the Transferrin saturation (TS) was calculated using the formula: $TS (\%) = [\text{serum iron (ug/dl)} / \text{serum transferrin (mg/dl)}]$ (Theodoros Eleftheriadis, et al. 2010)

Result: In anemic RA patients the MCV, MCH levels, serum iron, serum Ferritin, and TS% were significant decrease while there was a significant increase in platelets count compared to control.

Conclusion: Iron deficiency is common (77%) of anemic RA patients while there was (22%) of ACD. RA patients had lower serum iron, lower ferritin and lower TS%, while there was increase in platelets count, Decreased hemoglobin was the strongest determinants of iron deficiency.

Keywords: IDA anemia ,ACD, Rheumatoid arthritis;RA, Serum iron; ferritin; total iron binding capacity; TIBC, Transferrin saturation; TS%.

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Introduction:

Rheumatoid arthritis is a chronic autoimmune disease that affect hand and feet small joints causing swelling and bone erosion and joint deformity (2). Rheumatoid arthritis may occur at any age but the prevalence increases until age of 70. The disease Infects 1% to 2%of the adult

population and its incidence is greater in women than in men (3:1). Anaemia is the most common and serious blood abnormality seen in rheumatoid arthritis either anaemia of chronic disorder or iron deficiency anemia (3). Anemia of chronic disease. is a clinical entity, which is commonly observed in patients with various underlying diseases that

include anemia of chronic infection, anemia of cancer, anemia associated with rheumatoid arthritis, and anemia in chronic kidney diseases (4). Anemia associated with rheumatoid arthritis, known as rheumatoid anemia, is a typical example of anemia of chronic disease (5, 6). In the absence of effective treatment, anemia is highly prevalent among rheumatoid arthritis patients. The mechanisms involved in rheumatoid anemia include shortening of the erythrocyte lifespan, inadequate bone marrow erythropoiesis in response to the anemia, and iron metabolism abnormalities (5-7).

Materials and methods:

This a retrospective observation study was conducted in Khartoum State, between 2018 and 2021 sample collected from Military Hospital, Khartoum, Sudan and Modern Medical Center, Khartoum, Sudan. A total of 126 volunteers were enrolled in this study; 63 were Sudanese patients diagnosed with anemic RA as a patient's group; this study was approved by Omdurman Islamic University ethical committee. The consent was also taken from every participant before the samples were gathering. Five ml of venous blood were collected from all participants, and then measure CBC using sysmex Kx-21. The iron profile (serum ferritin, serum iron and total iron binding capacity) was carried out using automated Chemical analyzer Roche/Hitachi cobas c311 and

e411 (Roche Diagnostics GmbH, Mannheim, Germany). Transferrin saturation (TS) was calculated with the formula: $TS (\%) = [\text{serum iron (ug/dl)} / \text{serum transferrin (mg/dl)}]$. Data were collected by direct questioner and analyzed by using statistical package for social sciences (SPSS) version 23. T. test and ANOVA test were used. While Correlations between variables were evaluated by Spearman's correlation coefficient. The results were expressed as means + standard deviation. Significance was set at $P < 0.05$.

Results:

162 individuals were included in this study, 63 were patients with anemic rheumatoid arthritis and 63 were healthy as control group, the mean age of patients and controls were (46.04 ± 10.07) and 43.76 ± 3.91 years old, respectively).

The mean of Hb, RBCs, and HCT was significant decrease in case $(10.67 \pm 1.00, 4.38 \pm 0.540, \text{ and } 32.96 \pm 2.60, \text{ respectively})$ with $p.\text{value} = 0.00$

The mean of MCV and MCH was significant decrease in case $(76.07 \pm 7.52 \text{ and } 24.69 \pm 3.04, \text{ respectively})$ with $p.\text{value} = 0.00$, while there was insignificant increase in MCHC in case (32.35 ± 1.24) with $p.\text{value} = 0.07$. The mean of TWBC count was insignificant increase in RA (10.67 ± 1.00) , with $p.\text{value} = 0.1$ while there was significant increase in platelet count in RA patients (326.66 ± 108.62) , with $p.\text{value} = 0.04$

Table 1: Mean of age, CBC results among patients with rheumatoid arthritis compared to control

	Study population	Mean±STD	p.value
Age	Case	46.04±10.07	0.09
	Control	43.76±3.91	
Hb	Case	10.67±1.00	0.00
	Control	12.96±1.62	
WBC	Case	6.49±2.58	0.1
	Control	5.84±1.82	
RBC	Case	4.38±0.540	0.00
	Control	4.95±0.42	
HCT	Case	32.96±2.60	0.00
	Control	41.08±2.49	
MCV	Case	76.07±7.52	0.00
	Control	83.52±5.81	
MCH	Case	24.69±3.04	0.00
	Control	26.71±1.99	
MCHC	Case	32.35±1.24	0.07
	Control	31.98±1.08	
PLT	Case	326.66±108.62	0.04
	Control	291.73±79.20	

The mean $\pm$ STD of Serum Iron, Serum Ferritin, and TS% was significant decrease in case (5.66 $\pm$ 3.13, 14.45 $\pm$ 19.78, and 12.98 $\pm$ 11.29, respectively) with P.value = 0.00, while there was insignificant different in TIBC between case (50.68 $\pm$ 12.43) and control with P.value= 0.9.

Table 2: Mean of iron status among patients with rheumatoid arthritis correlated to control

	Study population	Mean $\pm$ STD	p.value
S. iron	Case	5.66 $\pm$ 3.13	0.00
	Control	16.09 $\pm$ 5.79	
S. Ferritin	Case	14.45 $\pm$ 19.78	0.00
	Control	28.24 $\pm$ 19.39	
TIBC	Case	50.68 $\pm$ 12.43	0.9
	Control	50.84 $\pm$ 5.43	
TS%	Case	12.98 $\pm$ 11.29	0.00
	Control	31.83 $\pm$ 10.58	

The correlation of different age group with CBC parameters were insignificant in the two age group of RA patients.

Table 3: Mean of CBC results among patients with rheumatoid arthritis correlated to age group

	Age (years)		p.value
	<40	>40	
Hb	10.37 $\pm$ 1.05	10.79 $\pm$ 0.97	0.1
WBC	5.77 $\pm$ 2.13	6.78 $\pm$ 2.71	0.1
RBC	4.27 $\pm$ 0.35	4.43 $\pm$ 0.59	0.2
HCT	32.00 $\pm$ 2.44	33.35 $\pm$ 2.58	0.06
MCV	75.89 $\pm$ 7.18	76.14 $\pm$ 7.73	0.9
MCH	24.55 $\pm$ 3.00	24.75 $\pm$ 3.09	0.9
MCHC	32.35 $\pm$ 1.19	32.36 $\pm$ 1.28	0.8
PLT	321.88 $\pm$ 103.39	328.57 $\pm$ 111.72	0.8

The correlation of different age group with Serum iron, serum ferritin, TIBC, and TS% were insignificant in the two age group of RA patients.

Table 4: Mean of serum iron, ferritin, TIBC and TS% among patients with RA correlated to age group

	Age (years)		p.value
	<40	>40	
Serum iron	5.75±3.86	5.62±2.84	0.8
Ferritin	12.26±18.58	15.33±20.38	0.5
TIBC	52.65±12.96	49.89±12.27	0.4
TS%	11.16±6.80	13.70±12.65	0.4

The Hb, WBCs, RBCs, MCV, MCH, MCHC, and PLT correlated to duration of disease were insignificant different in RA patients, while HCT was significant decrease with duration >10years compared to other group (p.value=0.04).

Table 5: Mean of CBC results among patients with RA correlated to duration of disease

	Duration (years)			p.value
	<5	5-10	>10	
Hb	10.84±.81	10.48±1.24	10.00±1.16	0.05
WBC	6.53±2.18	6.35±3.35	6.82±2.48	0.9
RBC	4.46±.49	4.28±.56	4.17±.87	0.1
HCT	33.42±2.30	32.41±2.83	31.25±3.64	0.04
MCV	75.6±7.4	76.95±7.79	76.3±9.08	0.6
MCH	24.63±3.03	24.88±3.12	24.37±3.49	0.9
MCHC	32.47±1.25	32.20±1.30	31.97±.970	0.3
PLT	336.46±120.82	315.95±92.56	284.75±17.03	0.3

The Serum iron, serum ferritin, TIBC, and TS% different compared to other group (p.value=0.3, correlated to duration of disease were insignificant 0.8, 0.2, 0.6 respectively).

Table 6: Mean of serum iron, ferritin, TIBC and TS% among patients with rheumatoid arthritis correlated to duration of disease

	Duration (years)			p.value
	<5	5-10	>10	
Serum iron	5.44±3.05	5.75±3.54	7.27±1.02	0.3
Ferritin	14.20±21.47	14.64±18.51	16.02±8.50	0.8
TIBC	49.18±12.36	52.66±12.82	55.32±11.55	0.2
TS%	13.77±13.57	11.34±6.55	13.45±2.42	0.6

Discussion:

This study was done to evaluate the CBC and iron profile in anemic Sudanese patients with Rheumatoid Arthritis. It was shown that Hb, RBCs, and HCT were significantly decreased in those cases, these outcomes match with the studies done by W.TAŃSKI 2021 (8), Tahani Mursal 2016 (9), Eman Tariq 2019 (10) and Abbas Sabbar Dkhil 2017 (11).

The Iron deficiency was common with 77% of anemic RA patients in current study, while it was 64% in the study done by W. TAŃSKI 2021(8), 60% by Wojciech Tański 2021 (12) and it was only 23% with the study done by Tahani Mursal 2016 (9).

The MCV and MCH were found to be significant decreased and the serum iron, serum ferritin and TS % were significantly decreased in RA Sudanese patients ,This agree with the studies done by Eman Tariq 2019 (10),W.TAŃSKI 2021 (8), Tahani Mursal 2016 (9) and Noha Mohamed Saeed 2016 (13).

Basak TB 2013 refer the decrease in the indices as

reflect of the iron deficiency anemia and explain the association between RA and iron deficiency (IDA) caused by gastrointestinal bleeding associated with drug treatment (14). Iron deficiency anaemia (IDA) is characterised by impaired haemosynthesis and the production of erythrocytes, which are smaller than normal and contain less haemoglobin as a result of iron deficiency, also reduced ferritin levels and transferrin saturation (TS) of less than 20% ,according to Wojciech Tański 2021, Babitt J.L 2010 and Franchini M.2010 all if these are due to excessive inflammatory activation and the resulting increased production of proinflammatory cytokines (mainly interleukin-6) and hepcidin (12) (15) (16)

There was a significant increase in platelet count in RA patients in this study which agree with the studies done by W. TAŃSKI 2021(8), and Li Xue 2022 (17).

ErtenliI explain that an increase in platelets count may be due to the action of particular interleukins, namely IL- 6 and IL-1, with pro-inflammatory

mediator activities which have been shown to be involved in the regulation of megakaryocytopoiesis (18) (19). Gasparyan AY 2010 showed the reactive megakaryocytopoiesis increases circulating platelets count, proinflammatory pleiotropic cytokines of RA also have megakaryocytopoietic / thrombopoietic properties (20). Abbas Sabbar Dkhil 2016 showed that platelets count, interleukin-6 IL-6 plays a major role in the pathogenesis of RA including thrombocytosis (21).

Conclusion:

Iron deficiency is common (77%) of anemic RA patients while there was (22%) of ACD.

RA patients had lower serum iron, lower ferritin and lower TS%, while there was increase in platelets count, Decreased hemoglobin was the strongest determinants of iron deficiency.

References:

1. Theodoros Eleftheriadis, et al. Which is the best way for estimating transferrin saturation?, Renal Failure, 2010; 32:8, 1022-1023
2. Neumann, et al. Rheumatoid arthritis progression mediated by activated synovial fibroblasts. Trends Mol Med., 2010; 16: 458–68.
3. Valier alcena, M.D. African Americans and medical disease an American health. Rheumatoid arthritis 2013: 399.
4. Jurado, RL. Iron, infections, and anemia of inflammation. Clin Infect Dis 1997; 25:888-95.
5. Gomollon, et al. Anemia and inflammatory bowel diseases. World J Gastroenterol 2009; 15:4659–65.
6. Masson, CJ. L'anémie rhumatoïde. Rev Rhum Mal Osteoartic 1992; 59(6 bis):30–65.
7. Means, RT. Hepcidin and anemia. Blood Rev 2004; 18:219–25.
8. W. TAŃSKI, et al. Iron metabolism in patients with rheumatoid arthritis. European Review for Medical and Pharmacological Sciences, 2021; 25: 4325-4335.
9. Tahani Mursal et al, differential diagnosis of anemia in rheumatoid arthritis sudanese patients. World Journal of Pharmaceutical and Medical Research .wjpmr, 2016,2(4), 01-04.
10. Eman Tariq Ali, et al.. A Comparative Study of Interleukin 6, Inflammatory Markers, Ferritin, and Hematological Profile in Rheumatoid Arthritis Patients with Anemia of Chronic Disease and Iron Deficiency Anemia. Hindawi Anemia Volume 2019, Article ID 3457347, 7 pages.
11. Abbas Sabbar Dakhil. Association of Serum Concentrations of Pro-inflammatory Cytokines and Hematological parameters in Rheumatoid Arthritis Patients. J. Pharm. Sci. & Res. Vol. 9(10), 2017, 1966-1974.
12. Wojciech Tański, et al. Anaemia and iron deficiency in patients with rheumatoid arthritis and other chronic diseases. (online), 2021; 75: 143-151 e-ISSN 1732-2693)
13. Noha Mohamed Saeed, et al. Evaluation of Iron Profile in Sudanese with Rheumatoid Arthritis. Journal of Medical and Biological Science Research Vol. 2016 2 (3), pp. 44-48.
14. Basak TB, et al. Anemia of chronic disease in rheumatoid arthritis and its relationship with disease activities. Dinajpur Med Col 2013; 6:113-22

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15. Babitt J.L., Lin H.Y.: Molecular mechanisms of hepcidin regulation: Implications for the anemia of CKD. *Am. J. Kidney Dis.*, 2010; 55: 726–741.
 16. Franchini M., Montagnana M., Lippi G.: Hepcidin and iron metabolism: From laboratory to clinical implications. *Clin. Chim. Acta*, 2010; 411: 1565–1569.
 17. Li Xue et al. Association Between Blood PLT and RBC Related Indices and Disease Activity in Patients with Rheumatoid Arthritis. *International Journal of General Medicine* 2022;15 573–581.
 18. ErtenliI, et al. Pathologic thrombopoiesis of rheumatoid arthritis. *RheumatolInt.*, 2003,23(2); 49-60.
 19. ErtenliI, et al. Cytokines affecting megakaryocytopoiesis in rheumatoid arthritis with thrombocytosis. *Rheumatol Int.*, 1996, 16(1); 5-8.
 20. Gasparyan AY, Stavropoulos-KalinoglouA, Sandoo A, and Kitas GD. Mean Platelet Volume in Patients with Rheumatoid Arthritis: the Effect of anti-TNF-alpha Therapy. *Rheumatology International*. 2010, 30(8); 1125-1129.
 21. Abbas Sabbar Dkhil et al .Association Between Interleukin-6(IL-6) and Thrombocytosis in Rheumatoid Arthritis Patient .*International Journal of PharmTech Research*, 2016,9(4),pp 307-312.)