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Yousif Adam Yousif Adam
Elshazali Widaa Ali
Khalid Abdelsamea Mohamed Ahmed
Nasr Eldeen Ali Mohammed Gaufri
Al-Neelain University

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Evaluation of Serum Iron and Total Iron Binding Capacity among Sudanese Patients with Rheumatoid Arthritis

Yousif Adam Yousif Adam[1*], Elshazali Widaa Ali[1], Khalid Abdelsamea Mohamed Ahmed[2], and Nasr Eldeen Ali Mohammed Gaufri[1]

[1]Dept. of Hematology, Faculty of Medical Laboratory Sciences, Al Neelain University, Khartoum, Sudan.
[2]Dept. of of Hematology and immunology, Faculty of Medical Laboratory Sciences, University of Gezira, Wad Medani, Sudan.

[*]Corresponding author E-mail: yousifadamyousif123@gmail.com.

Abstract

Background: Rheumatoid arthritis is a chronic autoimmune disease that affected small joint in the hand and feet causing swelling that can result in bone erosion and joint deformity, anemia is the most common and serious blood abnormality seen in rheumatoid arthritis. **Objectives:** This study aimed to evaluate the levels of serum iron, Total Iron Binding Capacity (TIBC) and Red blood cells parameters among Sudanese rheumatoid arthritis patients. **Material and Methods**: This is cross-sectional laboratory based study included 50 patient diagnosed by rheumatoid arthritis disease admitted to Omdurman Military Hospital, Khartoum, Sudan during period January to February 2020.Red blood cells parameters were determined using fully automated hematology analyzer (Sysmex N21).The serum levels of iron and TIBC were estimated using fully automated chemistry analyzer (Mendary BS200). Data were collected directly from each subject using direct predesigned questionnaire. Data were analyzed by SPSS statistical package of social science (SPSS version 21). **Results**: The present study showed that 68% of rheumatic were anemic patients (32%) were non-anemic. The frequency of the types of anemia showed that 35% of anemic rheumatoid arthritis patients have iron deficiency anemia and 64% have anemia of chronic disease. The mean of serum iron was statistically significant decreased among anemic rheumatoid arthritis compared with non-anemic rheumatoid arthritis patients (45.3 ug/dl ves 77.8 ug/dl with P value 0.00).Total iron binding capacity was significant decreased in anemic compared with those non anemic (270 ug/dlvis 212ug/dl with P value 0.00).The hematology parameters in this study Hb, MCV, MCH and MCHC levels were significant reduced in patients with Rheumatoid arthritis when compared to reference value with P value less than 0.05. **Conclusion**: Anemia of chronic disease was predominantly among Sudanese rheumatoid arthritis patients. Serum iron and total iron binding capacity were significant diminished among anemic rheumatoid arthritis compared with non-anemic rheumatoid arthritis patients.

Keywords: Irondeficiency, Rheumatoid arthritis, Anemia of chronic disorder, serum iron, total iron binding capacity, Sudan.

Introduction

Rheumatoid Arthritis (RA) is that the commonest sort of chronic inflammatory joint disease. It is an asymmetrical, non-supportive polyarticular disease. Rheumatoid arthritis affects the synovial joints but it's not confined to them and therefore the many visceral manifestations have led to the classification of RA as a systemic disorder of the immunological mechanism, of the systemic lesions, anemia and a focal subcutaneous granuloma are the most characteristics (Arul and Pravee, 2016). Anemia of chronic disease ACD and iron-deficiency anemia (IDA) are considered that the two commonest causes of anemia in RA (Hansen,1983).The difference in prevalence rate in various studies is said to the difference within the definition of anemia. Anemia adds considerably to the morbidity in patients with RA. Improvement in hemoglobin levels is associated with significant improvement in the quality of life of anemic patients with RA (Kaltwasser,et al 2001). Anemia of chronic disease is normocytic normochromic .the exact mechanisms underlying anemia of chronic disease (ACD) in RA is unknown but is possibly related to First, inflammatory cytokines, such as tumor necrosis factor (TNF)-a, interleukin (IL)-1b, and interferon, induce inadequate

erythropoiesis in bone marrow, inhibiting erythroid progenitor differentiation and driving the apoptosis of erythroid progenitors. Secondly, the inflammatory cytokines mediate the inhibition of peripheral iron utilization. Thirdly, the erythropoietin production in response to anemia is relatively impaired. Fourthly, red cell survival is slightly reduced in RA patients (Conrad,et al 1990 – Finch,1982). Iron deficiency anemia IDA is an anemia caused by a lack of adequate supplies of iron (Claudia,el at.2018). It is the most severe consequence of iron depletion, and it is still considered the most common nutritional deficiency worldwide. Although the etiology of IDA is multifaceted, it generally results when the iron demands by the body aren't met by iron absorption, no matter the rationale. Individuals with IDA have inadequate intake, impaired absorption or transport, physiologic losses associated with reproductive age, or chronic blood loss secondary to disease (Clark.2008). Iron deficiency anemia is usually microcytic hypochromic while anemia of chronic disease is normocytic normochromic (Weiss and Goodnough.2005). IDA in RA patients is attributed to iron deficiency, possibly caused by gastrointestinal bleeding associated with drug treatment or different malignancies (Skikne et al,2011).

Material and Methods:

This is a cross-sectional study conducted in Military Hospital Omdurman, Sudan from January to February 2020. Totally of 50 subjects were recruited for this study. All participants were patients known professionally diagnosed with rheumatoid arthritis. Based on gender 11(22%) male and 39(78%) were female, the mean age of our patients was 42.4 years old. Five ml of venous blood samples were taken from participants, 2 ml in a container contain ethylene-diethyl tetra acetic acid (EDTA) as an anticoagulant for hematological RBCs parameters analysis and other 3 ml in the plain container and centrifuged at 3000rpm for 5 minutes for serum preparation for serum iron and TIBC estimation. Hematological parameters hemoglobin level, HCT, MCH, and MCHC were done using full automated hematological analyzer Sysmex KXN-21. Biochemical parameters serum iron and Total Iron Binding Capacity (TIBC) were performed by using automated chemical analyzer Mendary BS200 (China). All tests done were compared with normal reference values. Every patient with chronic disease such (renal failure, heart disease, liver disease, Malignant diseases), or under iron therapy and who received blood transfusion were excluded from this study. This study was approved by Al-neelain university ethical board, and the approval consent also was taken from all participants before the samples were gathered. Data was collected by direct questionnaire then computed and analyzed by using a computer program statistical package for social sciences (SPSS) version 21. T.test was used to compare between the parameters and correlation between variables was assessed by using the Pearson test. P.value was set less than 0.05 were considered statistically significant.

Results:

Our analysis showed that anemia was present in 34 (68%) patients while 16(32%) were non-anemic Figure (1).

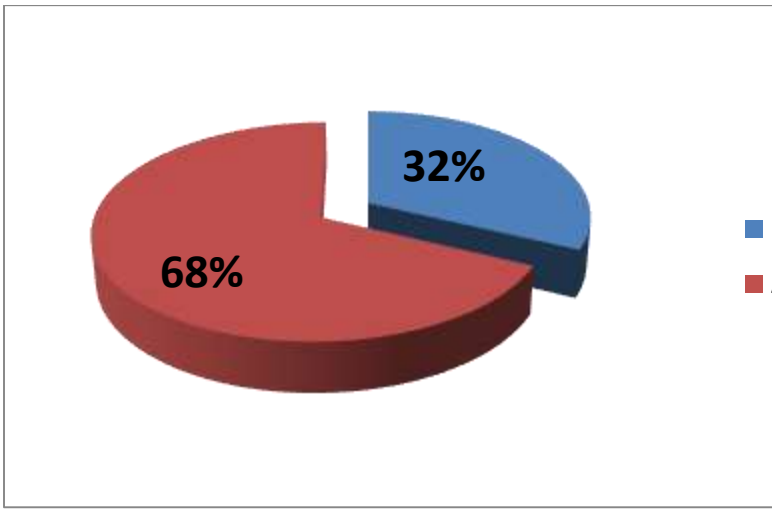

Figure1. Prevalence of anemia among rheumatoid arthritis patients.

In this study serum Iron, TIBC and hematological parameters (Hb, HCT, MCV, MCH, and MCHC) were measured and compared with the Reference values (Table 1).

Table1. Shows results of iron, TIBC and hematology parameters compared with Reference Value (RV).

Parameters	Mean	SD	Range	RV	*P value*
Hb g/dl	11.1	2.1	6.1-16.4	11.5-16.5	**0.000**
PCV %	33.9	6.1	19-49	40-52	**0.000**
MCVfl	80.3	11.8	18-95	80-95	**0.000**
MCH p.g	26.4	3.9	17.3-39.1	27-34	**0.000**
MCHC l/l	32.1	3.5	25.4-43	32-36	**0.001**
S. Iron ug/dL	55.2	21.3	9-122	50-170	**0.000**
TIBC ug/dL	250.3	52.7	121-398	150-330	**0.000**

Based on hemoglobin levels we classified our patients an anemic and non-anemic, this study revealed that mean of serum iron in anemic rheumatoid arthritis patients was 45.3 ug/dl, compared to 77.8 ug/dl in non-anemic rheumatoid arthritis patients this difference was found to be significant with (*P value* = 0.000). On the other hand our study showed that the mean of Total Iron Binding Capacity among anemic rheumatoid arthritis patients was statistical significant higher in comparison with non-anemic rheumatoid arthritis patients with (270ug/dl ves 212ug/dl with P value 0.00) (Table 2).

Table 2.Comparison of serum iron and TIBC between anemic and non-anemic rheumatoid arthritis patient.

Parameters	Anemia	Mean	SD	*P value*
S. Ironug/dL	Anemic	45.38	12.6	0.000
	Non anemic	77.81	20.6	
TIBC ug/dL	Anemic	270.00	47.2	0.000
	Non anemic	212.19	47.7	

According to types of anemia and depending to morphological features and, iron levels, this study found that 12 patients (35%) had Iron deficiency anemia and 22 patients (64%) had anemia of chronic disease. Figures (2)

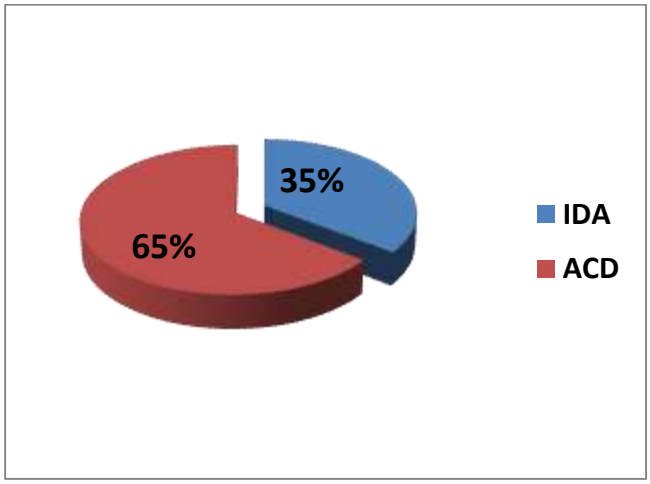

Figure 2. Prevalence of IDA and ACD among rheumatoid arthritis patients.

The current study found that a strong positive correlation between Hb,PCV,serum iron and TIBC with the duration of Rheumatoid Arthritis disease with P value less than 0.05.

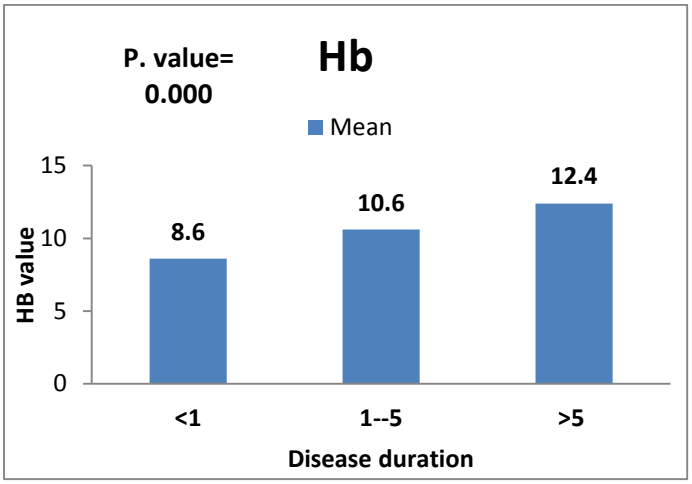

Figure 3. Correlation between Hb levels and duration of RA.

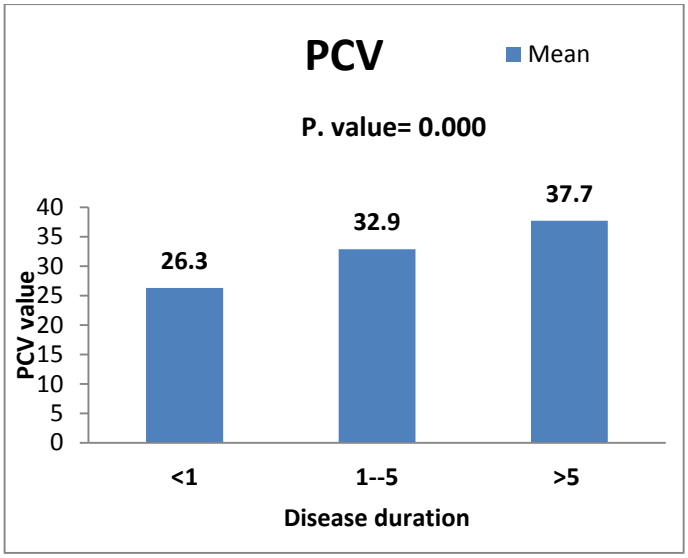

Figure 4. Correlation between PCV levels and duration of RA.

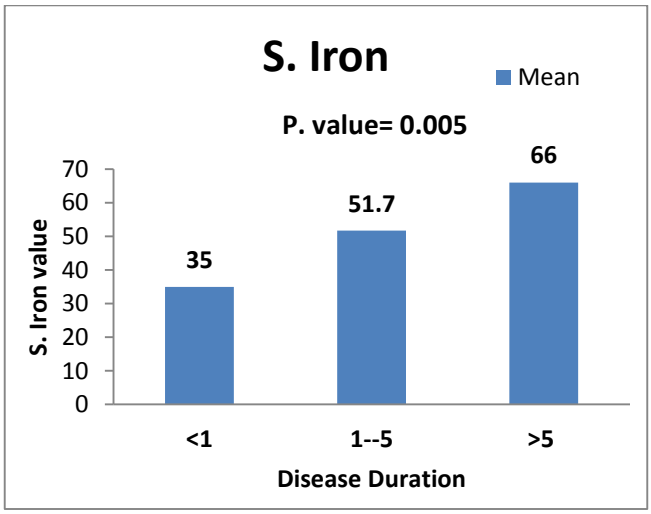

Figure 5. Correlation between S. iron levels and duration of RA.

Discussion:

Iron is the most critical for the normal functioning of various biological processes in all kingdoms. It is an essential component of several biochemical reactions, including oxygen transport, enzyme catalysis, and photosynthesis (Silva el at 2015). Inflammation-associated with hypoferremia compromises erythropoiesis by restricting the amount of iron available for hemoglobin synthesis. In addition, inflammation can directly obstruct RBC generation (Smriti el at , 2017).

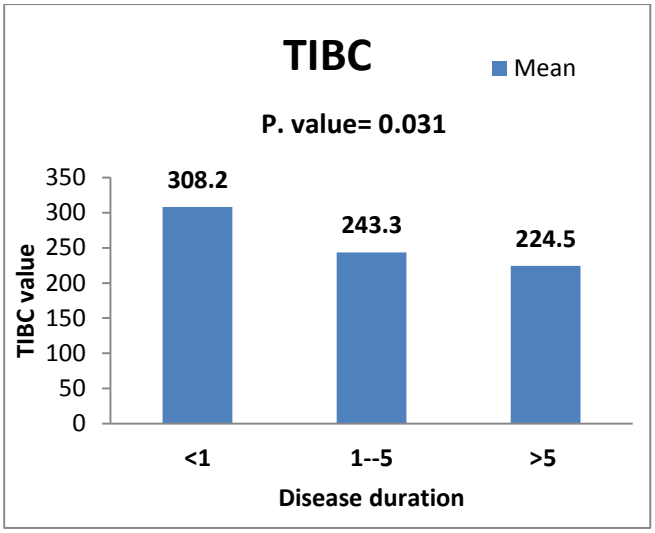

Figure 6. Correlation between TIBC levels and duration of RA.

This study aimed to evaluate the levels of serum iron, Total Iron Binding Capacity (TIBC), and hematological parameters levels (Hb, HCT, MCH, MCHC) among Sudanese rheumatoid arthritis patients. The current study showed that (68%) of Sudanese rheumatoid arthritis patients had anemic status. This finding was in agreement with a study done (2009) in which the author demonstrates 10,397 patients, and found that1734 (16.7%) had decreased the Hb levels (Furst,el at ,2009). Our finding also in the same line as the recent study done in China (2020) in which 890 RA patients were studied and concluded that anemia was observed in 47% of the RA patients (Chen,et al,2020). The relationship between rheumatoid arthritis and anemia was well documented (Han,et al, 2007. Hove.et al , 2000). Among anemic rheumatoid arthritis patients, this study shows that (35%) had Iron deficiency anemia, and (64%) had anemia of chronic disease. This finding similar to that reported the common hematological change during rheumatologic disorders are the anemia of chronic disease (ACD), and iron deficiency anemia (Baer,et al,1990). Despite the causes of anemia in rheumatoid arthritis not clear yet, but most agreed that increased expression of hepcidin is the foremost factor in the abnormal iron metabolism associated with inflammation (Sharma et al , 2005).Top of FormBottom of FormSeveral biomarkers of iron status have been done in a clinical setting. However, traditional biochemical iron parameters such as serum iron and serum ferritin are influenced by inflammation (Suchdev el at 2017). In

the current study, the hematological parameters (Hb, HCT, MCH, MCHC) serum iron and total iron-binding capacity were statistical significant decreased, and this finding was in agreement with study that evaluate and assessed hematological and biochemical tests among Eighteen patients diagnosed with rheumatoid arthritis and reported that (36%) had IDA and (64%) had ACD, on the other hand, the mean corpuscular hemoglobin (MCH), serum iron, TIBC and mean corpuscular hemoglobin concentration (MCHC) were reduced(Ravindran et al ,2008). Consistency with previous studies done in Glasgow-UK and India (Porter, et al ,1994 - Agrawal et al ,2006).

This study revealed that a positive correlation between Hb, PCV, serum iron, and TIBC with the duration of Rheumatoid Arthritis disease with P value less than 0.05, this result was matched with the study of Saeed et al (2016) in Sudan, who estimates the Serum level of Iron, TIBC and blood indices (Hb, HCT, MCH, and MCHC) and compared with the Reference values (R.V), and concluded that these parameters were significantly decreased, also reported that positive correlations between MCHC, HCT, Hb and duration of rheumatoid arthritis disease(Noha ,et al ,2016). Although the bone marrow iron stain and serum transferrin receptor analysis are most reliable in the diagnosis of iron deficiency in patients with RA but didn't make which might be considered one of the limiting factors of this study (Fitzsimons and Brock , 2001).

Conclusion:

According to our result, this study concludes that the hematological parameters (Hb, HCT, MCH, and MCHC) and biochemical markers serum iron and iron-binding capacity were statistically significantly reduced among Sudanese rheumatic arthritis in comparison with the normal reference value. Also, there is a positive correlation between Hb, HCT, serum iron, and TIBC with the disease duration.

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