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Evaluation of Iron Profile in Sudanese with Rheumatoid Arthritis

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ABSTRACT

Anemia adds considerably to the morbidity in patients with rheumatoid arthritis (RA). Iron has many important functions in human body. This study aimed to evaluate the level of blood indices, serum Iron and Total Iron Binding Capacity (TIBC) and their correlation with durations and complications of disease. This is cross-sectional study involved 48 patients with rheumatoid arthritis disease. The serum level of iron and total TIBC were estimated by the automated chemistry analyzer (COBAS-plus 400), blood indices by automated hematology analyzer (Sysmex). The analysis of the results indicated that the means level of iron, TIBC, hemoglobin, mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC) were significantly lower than the reference value, while hematocrit (HCT) results revealed insignificant change. Positive correlations were found in MCH, HCT and duration of disease. All hematology parameters levels were insignificantly correlated with complication of disease. The results observed that the levels of serum iron, TIBC, MCH and Hb was significantly decreased in patients with Rheumatoid arthritis when compared to reference value. Insignificant correlation observed between level of these elements and complication of RA disease, and significantly increases level of HCT, MCH in long duration patient group.

Key words: Rheumatoid, Iron, TIBC and Sudan.

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic articular inflammation and progressive joint destruction that releases most prominent manifestations in the diarthrodial joints (Michael et al., 2010). Among the most common hematologic abnormalities in patients with rheumatologic disorders is the anemia of chronic disease (a mild anemia that is generally asymptomatic) and iron deficiency anemia (Wilson et al., 2004; Baer et al., 1990). In patients with RA, the prevalence of anemia ranges from 30 to 70% in various studies (Baer et al., 1990). Anemia is a common morbidity in patients with RA (Hansen, 1993). Many of symptoms are present before its diagnosis. Weight loss, fever, prolonged early morning stiffness, fatigue, generalized muscle weakness, low mood, and depression are often responsible for a significant loss in the quality of life of patients. Fatigue is reported in 40 to 80% of RA patients as their most disabling symptom (Hansen, 1993), anemia of chronic disease (ACD) and Iron deficiency anemia (IDA) are two most important types of anemia and often occur concurrently (Lawrence, 1998).

Iron deficiency anemia is usually microcytic hypochromic while anemia of chronic disease is normocytic normochromic (Balsamo et al., 2014). 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). Anemia adds considerably to the morbidity in patients with RA. Improvements in hemoglobin levels are associated with

Table 1. Shows results of iron, TIBC and hematology parameters (RA patients, no = 48).

	Range	Median	Mean ±SD	R.V	*P.Value*
S. Iron	3.7 - 163	58.10	62.7± 31	35 -145	0.00
TIBC	191- 434	290.70	301 ± 57.3	619-1953	0.00
Hb	6.3 - 15.7	12.35	12.2± 2.2	11-16	0.00
HCT	19.9 – 51.6	37.00	37.5±8.8	37 – 54	0.67
MCH	20.2 – 32.1	28.20	28 ± 2.2	27 – 34	0.004
MCHC	28.7 – 37.4	32.60	33.2±4.9	32 - 36	0.031

R.V: Reference value.

significant improvement in quality of life of anemic patients with RA (Hove et al., 2000). Iron is extremely vital to the human beings because of its indispensable role in oxygen transport, DNA synthesis and electron transport (Bloxham et al., 2001). Consequently vital body functions are conditional on appropriate iron stores. Hemoglobin synthesis is particularly iron dependent (Kaltwasser et al., 2001). There are possible mechanisms in the anemia of chronic inflammatory diseases in RA. First, inflammatory cytokines, such as tumor necrosis factor (TNF)-a, interleukin (IL)-1b and interferon-g, 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. Forthly, red cell survival is slightly reduced in RA patients (Conrad et al., 1999; Finch et al., 1982).

In general, a degree of anemia correlates with RA disease activity and serum TNF-a concentration (Bowman et al., 2002). It is associated with decreased serum iron and TIBC, but iron store is increased or normal. Iron deficiency anemia due to long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) and folate deficiency due to methotrexate therapy also result in the anemia in RA (Bertero et al., 2011).

MATERIALS AND METHODS

In this cross-sectional study, carried out on 48 (4 males and 44 females) patients with RA disease, age range (18 to 75 years) from Academic Hospital, KRT Sudan. All participants were selected by physician rheumatologist and fulfilled the American's College of Rheumatology Revised (ACR) criteria (Arnett et al., 1987). Blood sample (5 ml) from all patients was collected with sterile syringe, under aseptic and antiseptic condition, withdrawal and mixed in lithium heparin containers, separated by centrifuge at 3000 to 4000 rpm. The plasma was obtained by centrifugation of blood at 3000 rpm for 10 min and stored at -20°C till used.

Ethical Considerations

The study has been approved by the local ethics committee of Medical Laboratory Sciences, Al-Neelain University. All participants in the study had signed written informed consent considering the aims of the study, samples and clinical information were used anonymously.

Estimation of Iron and Total Iron Binding Capacity

COBAS INTEGRA 400 plus analyzer is an advanced integrated system for diagnostic clinical chemistry testing classical chemistry. This system was used to estimate iron and TIBC. Automated hematology analyzer (Sysmex. KX-21) was used for complete hemogram (Hemoglobin, HCT, MCH and MCHC).

Statistical Analysis

Data were analyzed by SPSS statistical package of social science (version 16.0; SPSS Inc.). The Paired t-test was employed to compare differences between the means of continuous variables and Pearson's correlation to correlate between study parameters and variables. *P*-values less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

This study involved 48 patients with RA disease. Serum level of Iron, TIBC was measured as well as the blood indices (Hb, HCT, MCH, and MCHC) compared with the Reference values (R.V) shown with the patients characteristics in (Table 1).The reference range value of Hb is (11 to 16 gm/dl), HCT= (37 to 54%), MCHC= (32 to 36 mg/dl), MCH= (27 to 34 mg/dl), serum IRON =(35 to 145 ug/dl) TIBC =(619 to 1953 ug/dl). Figure 1 presents positive correlations between the levels of HCT and duration of RA disease, r=0.358*, p.value*=0.012, whereas between MCH level and duration r=0.37, *p.value*=0.009 Figure 2. Figure 3 shows also positive correlations between MCHC and duration of RA disease, and

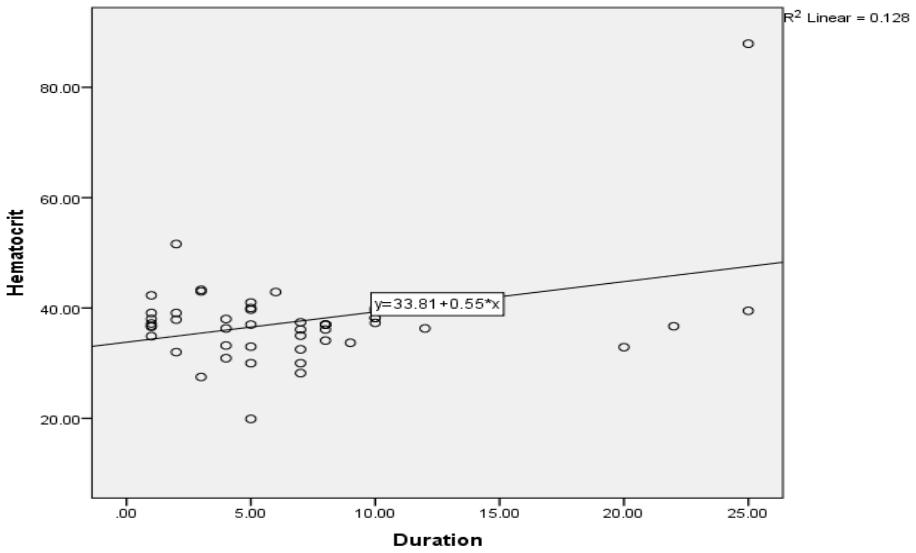

Figure 1. Shows correlation between HCT levels and duration of RA.

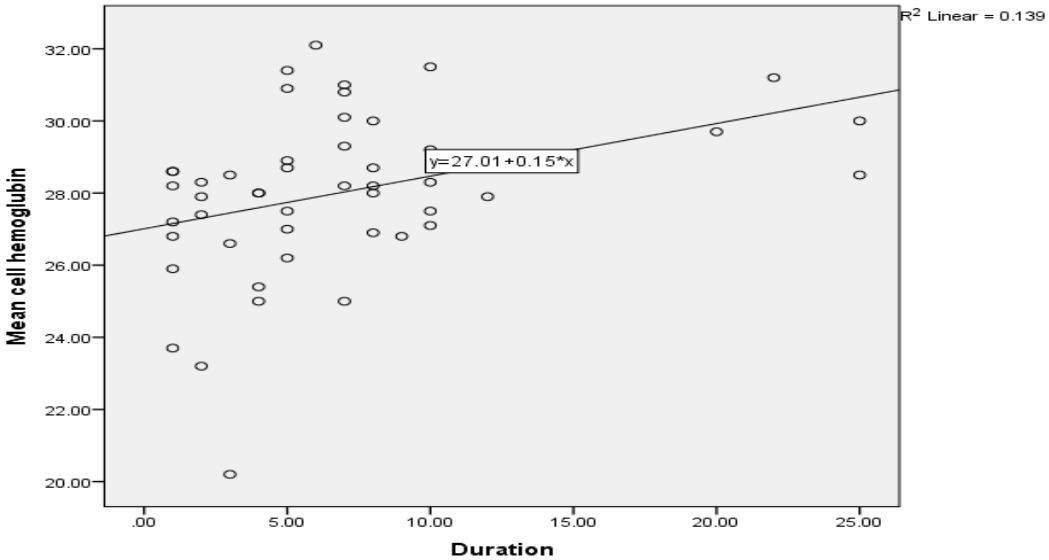

Figure 2. Shows positive correlation between MCH and duration of RA.

between Hbr versus HCT, r was (0.35, 0.791 and *p.value* was 0.015, 0.000), respectively (Figures 3 and 4).

This study aimed to evaluate the hematological parameters levels (Hb, HCT, MCH, MCHC, Iron and TIBC) in RA patients as well as to study correlations between these with complications and durations of RA disease. The role of iron in chronic inflammatory states is of great interest because there was a demand for it, and Iron is extremely vital to the human beings and of its indispensable role in oxygen transport, DNA synthesis and electron transport (Bloxham et al., 2001). The present study demonstrates that, the mean levels of Hb, MCH, MCHC, IRON and TIBC were significantly decreased in the RA patients when compared with reference values, p.value (0.000, 0.004, 0.031, 0.00 and 0.00), respectively. The obtained results of Hb was in consistent to that of previous study (Bowman et al., 2002), Anemia adds considerably to the morbidity in patients with RA, thus improvement in hemoglobin levels is associated with significant improvement in quality of life of anemic patients with RA (Hove et al., 2000).

Anemia in RA patients may be due to; improper iron utilization with decreased serum iron and transferrin concentrations, reduced erythropoietin levels, decreased bone marrow response to erythropoietin, premature destruction of red blood cells or due to the drugs used in

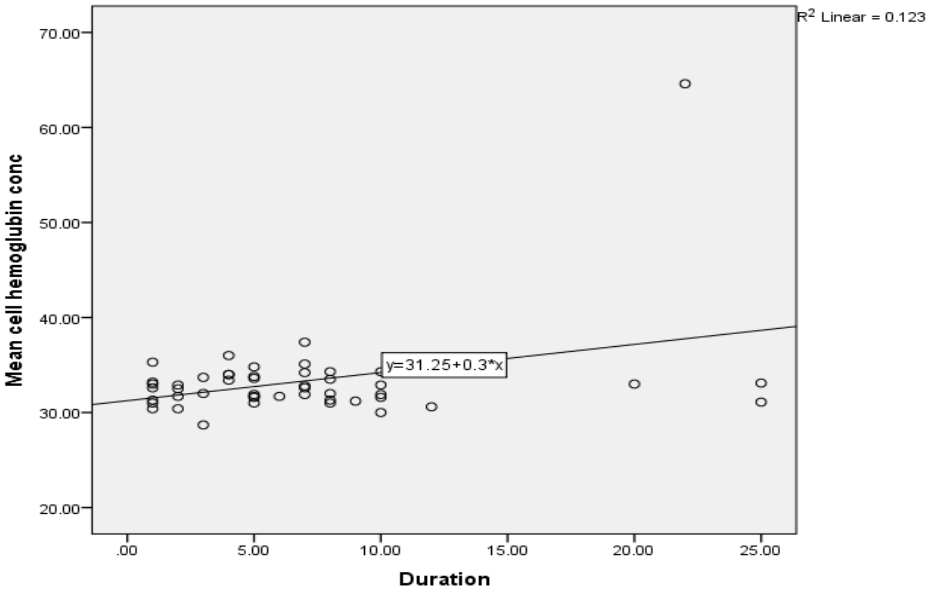

Figure 3. Shows positive correlation between MCHC and duration of RA**.**

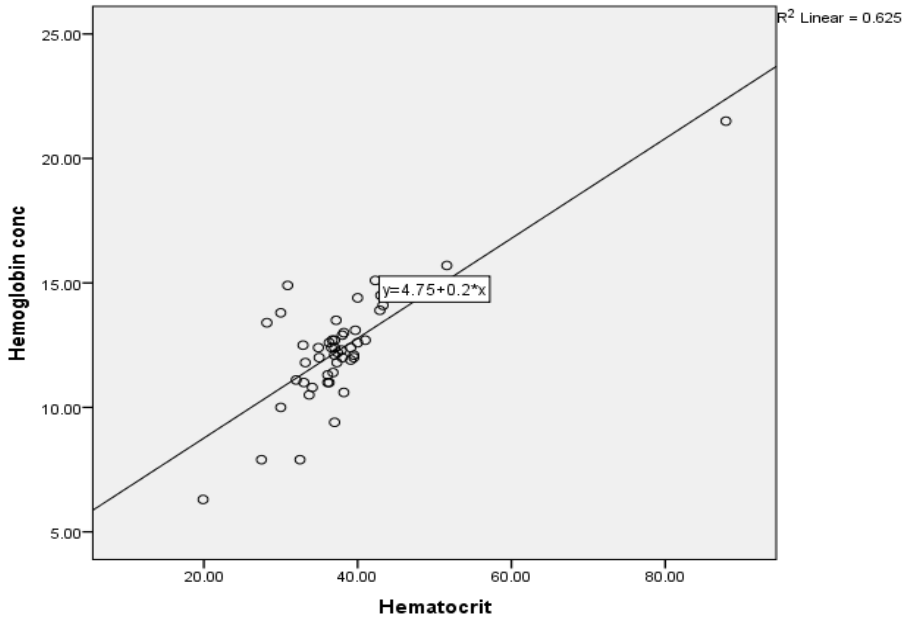

Figure 4. Shows positive correlation between haemoglobin and HCT in RA.

the treatment of RA patients as non-steroidal anti-inflammatory drugs and methotrexate (Bowman et al., 2002; Arnett et al., 1987). The result of this study was in agreement with of previous study (Porter et al., 1994), who found significantly lower MCH and MCHC p.value=(0.001, 0.001). In this study, serum iron and TIBC were significantly decreased among patients, similar to the report in the past research study (Ravindran et al., 2008), who said that the leading cause of the anemia in RA is chronic inflammation. It is associated with decreased serum iron and TIBC, but iron store is increased or normal. Iron deficiency anemia due to long-term use of NSAIDs and folate deficiency due to methotrexate therapy also result in the anemia in RA. Some cases demonstrate true iron deficiency while other anemic subjects have normal iron stores and the serum

total iron-binding capacity is not raised. It has been suggested that iron absorption is defective (Wilson et al., 2004).

In another study (Roberts et al., 1963) divided the RA disease in to 3 groups (IDA, ACD, non-anemic) and compared with control groups, iron was found significantly lower and TIBC inconsistent with our finding results was found significantly higher (Agrawal et al., 2006). In this study comparison between mean level of hematological parameters (MCH and HCT) was significantly increased in the long duration group rather than others, among the patients of RA disease, revealed statistical significant higher levels of MCH between the durations (less than 5 years and 5 to 10 years) and (less than 5, greater than 10 years) p.value was (0.001 and 0.013), respectively, and significantly higher levels of HCT between duration (5 to 10, greater than 10 years) presented *p.value* 0.03). Our results revealed a prevalence of anemia among the RA patients of 47.9%, although some other researchers reported a prevalence of 26.9% to 77.6% in patients with RA (Vreugdenhil et al., 1990). Correlations of hematology parameters considered a significant positive correlation between the levels of HCT and duration of RA disease, r=0.358, *p.value*=0.012 (Figure 1), whereas between MCH level and duration r=0.37, *p.value*=0.009 Figure 2, as well as between MCHC and duration of RA disease, and between Hb versus HCT, r. values were 0.35, 0.791 and *p.value* were 0.015, 0.000 respectively (Figures 3 and 4).

CONCLUSIONS AND RECOMMENDATIONS

The results observed that the mean levels of plasma iron, TIBC, Hb, MCH and MCHC were significantly decreased in patients with Rheumatoid arthritis when compared to references value. Insignificant correlation observed between level of these elements and complications of RA disease, and significantly increases level of HCT, MCH in long duration patient group. Supplementation with folic acid would be necessary for RA patients, because low iron lead to anemia.

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