



Study the Associated of Rheumatoid Arthritis with Anemia and Lipid Profile Changes in the Men and Women Patients in the Holy City of Karbala

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ABSTRACT

Objective: The aim of the current study is to find out the relationship between Rheumatic Arthritis with anemia and lipid profile changes in the men and women Patients in the Holy City of Karbala.

Methods: In the present study 20 healthy voluntaries divided in to two groups (each 10, males and females), and 20 patient divided in to two groups (each 10, males and females), Lipid Profile and hematological parameter measured.

Results: Males RA patients showed significant increase in the level of TC ($P \leq 0.05$) LDL ($P \leq 0.02$), VLDL ($P \leq 0.02$), TG ($P \leq 0.01$) while the result found significant decrease in the level of HDL ($P \leq 0.04$). In females RA patients showed significant increase in the level of TC ($P \leq 0.05$) LDL ($P \leq 0.001$) and highly significant decrease in the level of HDL ($P \leq 0.001$). Data showed significant decrease in serum ferritin of males RA ($P \leq 0.05$), highly significant increase ($P \leq 0.001$) in ESR for male and females RA. Result found significant decrease in Hb for both males and females RA as compared to control. The result revealed significant decrease ($P \leq 0.01$) in the RBC count for females RA patients. Study found significant decrease in platelets and MCV for males and females RA patients.

Conclusion: dyslipidemia was observed in RA is a frequent occurrence and may be considered as a secondary impact of chronic inflammatory state seen in RA patients, also serious hematological abnormalities violations that can be caused by the activity of the disease were revealed.

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease; RA was first recognized in 1859 by (Dr. Archibald Garrod) when he described widespread joint pain and stiffness¹. The prevalence of

RA, at 0.5–1%, is relatively constant in many populations but factors such as gender, race and smoking status can cause a variation in this prevalence rate². The etiology of RA Although is not fully

understood it may be due to a complex of genetic, endogenous factors (e.g. endocrine, hormonal, or metabolic factors) and exogenous factors (e.g. infectious agents, geographic, or occupational factors) ³. Recent studies revealed that mediators of inflammation such as cytokines play a key role in the development of RA ⁴. RA causes increased rates of mortality and morbidity which can be attributed to risk factor of cardiovascular disease (CVD) linked to coronary atherosclerosis ⁵. Recent study found the relation between these inflammatory diseases and other complications, such as anemia, infection inflammatory bowel disease and pulmonary tuberculosis ⁶. Multiple systemic symptoms developed with (RA) including fever, fatigue, anemia, anorexia, osteoporosis, weight loss, and muscle weakness ⁷. Other study demonstrated that IL-6 plays a crucial role in its pathogenesis, in addition to many risk factors such as obesity, smoking, diabetes, physical inactivity and hypertension, two things accelerated atherosclerosis in RA: the first one when being chronic inflammatory state and the other dyslipidaemia ⁸. In 30-70% of RA patients developed anemia, there are many types of anemia, including anemia of chronic disease (ACD), iron deficiency anemia (IDA), the combination of IDA and ACD (COMBI) anemia, hemolytic anemia and megaloblastic anemia have been seen in RA patients ⁴. Furthermore, evidence suggests that anemia of chronic disease (ACD) seen in up to 50% of RA patients ^{9, 10}. The metabolic process of lipid is a complex; therefore in many autoimmune diseases lipid abnormalities are commonly seen ¹¹. The dyslipidemia found in RA patients when showed high total cholesterol (TC) and low HDL, which is an important prognostic marker for cardiovascular disease (CVD) ¹². Recently, a great interest has been found between RA Tunisian patients and lipid tests, which record high level of LDL, TC and TG while low level of HDL and this mainly related to atherosclerosis and myocardial infarction ¹³. There are many researches showed prevalence of dyslipidaemia in 87 patients with inflammatory arthritis ¹⁴.

MATERIALS AND METHODS

Study Design

The present study conducted at the 'Rheumatology Clinic in AL-Hussein hospital of holy city Karbala, and the samples were collected from July to September 2017.

Patients

The patient was not exposed to any treatment and randomly divided to 4 groups, 10 people to each as follow:

- RA patient group: divided in to two groups (10 females and 10 males).
- Control group: (10 females and 10 males) for each one.

Sample Collection

Blood samples were collected in a sterile manner tubes after an overnight fasting. 5 ml of vein blood was drawn divided into 2.5 ml for sterile (EDTA) tubes, and 2.5 ml into free anticoagulant tubes allowed to clot for 30

minutes at room temperature, and then the serum was separated by centrifugation at 3000xg for 15 minutes and immediately frozen at -20 °C until tested.

Laboratory Measurements

Hematological test: The complete blood count test (CBC) was then measured electronically by (Mindray BC-3000Plus device) and this include RBC, WBC, Hg, PCV, MCV, MCH, MCHC and Platelets.

The erythrocyte sedimentation rate (ESR), was done according to the modified method of Westergren.

Biochemical test: Lipid profile test: Total cholesterol (TC), High density lipoprotein (HDL), light density lipoprotein (LDL), very light density lipoprotein (VLDL) and triglyceride (TG) levels were determined by enzymatic methods, were measured via (Cobas c311) device.

Serum ferritin: the ferritin levels were measured via (Cobas c311) device.

Statistical Analysis

Data were analyzed using Software; the differences between groups were measured by using *T-test* ¹⁵.

RESULTS

The result of present study showed significant differences in the all lipid profile parameters of male patients with RA as compared to the control group, **Table 1**. The study revealed significant differences in total cholesterol (TC), LDL and HDL of the female patients with RA as compared to the control group, while no any significant differences in the level of VLDL and TG, **Table 2**. The results of **Table 3** revealed that no any significant differences in the all parameters of lipid profile as compared between males and females patient with RA. The results showed significant differences in the blood parameters (serum ferritin, ESR, Hb, MCV and PLT) of male patients with RA as compared to the control group. On other hand no any significant differences in parameters (RBC, WBC, MCH and MCHC) **Table 4**. The results of present study revealed no any significant differences in the level of serum ferritin, WBC, MCHC), while found significant differences in the level of (ESR, Hb, RBC, MCV, MCH and PLT) in female patients with RA as compared to the control group, **Table 5**. The results of present study showed significant differences in the level of (serum ferritin, RBC and PLT), while found no any significant differences in the level of (ESR, Hb, WBC, MCV, MCH and MCHC) as compared between males and females patients infected with RA, **Table 6**. The results showed that the highest in the frequency and percentage of the male patients with RA occur in the age with range (48-61years), while the lowest in the frequency and percentage occur in the age with range (62-75years), **Table 7**. The results revealed that the highest frequency and percentage of the females patient with RA occur in the age with range (48-61years), while the lowest frequency and percentage occur in the age with range (20-23years) and (34-47years), **Table 8**.

Table 1: Study the lipid Profile parameters in male patients of Rheumatoid Arthritis as compared to the control group.

Parameters	Control	Male Patients	P value
Total cholesterol (mg/dl)	140.41 ± 5.50	196.9 2± 12.04	P≤ 0. 05
LDL (mg/dl)	75.89 ± 14.29	141.85 ±13.89	P≤ 0.02
HDL (mg/dl)	57.07 ± 3.38	36.94±4.28	P≤ 0.04
VLDL (mg/dl)	14.47 ±2.29	22.33 ± .70	P≤ 0.02
Triglyceride (mg/dl)	72.29± 11.47	111.43± 13.33	P≤ 0.01

Table 2: Study the of lipid profile parameters in female of Rheumatoid Arthritis patients as compared to the control group.

Parameters	Control	Female Patients	P value
Total cholesterol (mg/dl)	173.95 ±18.20	199.56 ± 5.62	P≤ 0.05
LDL (mg/dl)	75.20±5.09	149.86± 6.603	P≤ 0.001
HDL (mg/dl)	59.15 ±3.106	38.87 ± 3.08	P≤0.001
VLDL (mg/dl)	17.05 ± 2.01	20.56 ± 1.93	P≤ 0.11
Triglyceride (mg/dl)	86.27 ±9.57	102.94 ±9.66	P≤ 0.11

Table 3: Comparison study for lipid profile parameters between male and female patients infected with Rheumatoid Arthritis.

Parameters	Male Patients	Female Patients	P value
Total cholesterol (mg/dl)	196.92 ±12.04	199.56 ±5.62	P≤0.16
LDL (mg/dl)	141.85 ±13.89	149.86 ±6.60	P≤0.30
HDL (mg/dl)	36.94±4.28	38.87 ± 3.08	P≤0.11
VLDL (mg/dl)	22.33 ±2.70	20.56 ±1.93	P≤0.30
Triglyceride (mg/dl)	111.43 ±13.33	102.94 ±9.66	P≤0.30

Table 4: Study the effect of Rheumatoid Arthritis on some blood parameters in male patients as compared to the control group.

Parameters	Control	Male Patients	P value
Serum ferritin (ng/ml)	36.87 ±7.93	21.50 ±1.52	P≤0.05
ESR (mm/hr)	11.6±2.1	92±7.34	p≤0.001
Hb g/dl	13.67 ±0.70	11.84 ±0.52	P≤0.02
RBC(cell\ml ³)	4.40 ±0.30	3.74 ±0.34	P≤0.3
WBC(cell\ml ³)	8.40 ±0.76	7.31 ±0.58	P≤0.15
MCV(fL)	101.17 ±3.039	88.80 ±2.22	P≤0.001
MCH (Pg)	32.00 ±1.95	33.41 ±1.60	P≤ 0.18
MCHC (g/dl)	35.70 ±1.43	37.61±2.81	P≤0.4
PLT(10 ³ /uL)	227.80 ±17.90	188.00 ±11.17	P≤0.03

Table 5: Study the effect of Rheumatoid Arthritis on some blood parameters in female patients as compared to the control group.

Parameters	Control	Female Patients	P value
Serum ferritin (ng/ml)	42.04 ±7.51	30.60 ±3.70	P≤0.2
ESR (mm/hr)	25.00 ±5.32	99.00 ±5.41	P≤0.001
Hb g/dl	12.04 ±0.44	10.83 ±0.22	P≤0.01
RBC(cell\ml ³)	4.10 ±0.23	3.24±0.21	P≤0.01
WBC(cell\ml ³)	7.00 ±0.64	6.90 ±0.20	P≤0.3
MCV(fL)	99.13±1.04	85.30±2.56	P≤0.01
MCH (Pg)	33.00±3.26	38.28±2.84	P≤0.07
MCHC (g/dl)	36.50±2.27	39.10 ±2.26	P≤0.13
PLT(10 ³ /uL)	300.30 ±41.64	138.40±12.97	P≤ 0.001

Table 6: Comparison study for some blood parameters of male and female patients infected with Rheumatoid Arthritis.

Parameters	Male Patients	Female Patients	P value
Serum ferritin (ng/ml)	21.50 ±1.52	30.60 ±3.70	P≤0.01
ESR (mm/hr)	92.00 ±7.34	99.00 ±5.41	P≤ 0.16
Hb g/dl	11.84±0.52	10.83 ±0.22	P≤0.07
RBC(cell\ml ³)	3.74 ±0.34	3.24 ±0.21	P≤ 0.03
WBC(cell\ml ³)	7.31 ± 0.58	6.90 ± 0.20	P≤ 0.3
MCV(fL)	88.80 ± 2.22	85.30 ± 2.56	P≤ 0.4
MCH (Pg)	33.41 ±1.60	38.280±2.84	P≤ 0.09
MCHC (g/dl)	37.61 ±2.81	39.10 ±2.26	P≤ 0.2
PLT(10 ³ /uL)	188.00 ±11.17	138.40 ±12.97	P≤0.005

Table 7: Comparison study for some blood parameters of male and female patients infected with Rheumatoid Arthritis.

Age	Frequency	Percent
20 - 33	1	10.0%
34 - 47	3	30.0%
48 – 61	4	40.0%
62 - 75	0	00.0%
76 – 89	1	10.0%
<90	1	10.0%

Table 8: Study the age Distribution in the female patient with Rheumatoid Arthritis.

Age	Frequency	Percent
20 - 33	1	10.0%
34 - 47	1	10.0%
48 – 61	5	50.0%
<62-75	3	30.0%

Discussion

Rheumatoid arthritis (RA) is a chronic autoimmune disease. It causes joints to swell and can result in pain, stiffness, and progressive loss of function ⁷. The results of present study showed significance increase in the lipid profiles (LDL, VLDL, TC, TG), while there is significance decrease of HDL of males patients infected with RA, this result can be related to the suppression of TNF α and lipid metabolism, in keeping with our results, many studies documented that TNF α has the capacity to induce dyslipoproteinemia by stimulating production of LDL and triglyceride, TNF α is stimulate cholesterol biosynthesis through induction of maturation of sterol regulatory element binding protein-1 (SREBP-1), also increased free fatty acid production and induction of lipolysis ¹⁶. Hyperlipidemia may be related to the role of IL-6 which causes activated VLDL receptor and delivery of fatty acids, also IL-6 has lipolysis properties and increases lipolysis of adipose tissue and adipocytes⁷. The present study in agreement with what found by ¹¹ they showed significant increase in the level of TC and LDL. Also another study formed by ¹⁷ demonstrated that atherogenic lipid profile includes decreased HDL and increased TC, LDL in serum levels suggesting that these

patients are possibly exposed to a higher risk of atherosclerosis. As well as present study in agreement with what found by ¹ who revealed that markedly decreased in the level of HDL, LDL and VLDL in rheumatoid arthritis patients as compared to normal values in control. The same result found that lower levels of HDL and TC, higher LDL in active or untreated disease than in general population ^{7, 18}. On other hand the present study disagreement with what found by ¹⁹. The results of present study showed significant decreased of HGB, RBC and serum ferritin in male patients, while there is normal serum ferritin of females patient and the causes of this decreased may be related to: Changes in iron metabolism are the leading causes of anemia in RA patients another reason may be related to inflammatory cytokines which play important roles of RA anemia ⁷. On other hand Hcpidin hormone is a master regulator of iron, the main functions are inhibits the absorption of iron in the small intestine and the release of recycled iron from macrophages and decreasing the delivery of iron to maturing erythrocytes in the bone marrow ²⁰. Present study in agreement with ² showed iron-restricted erythropoiesis in anemia can be attributed to the excess Hcpidin levels. Another study demonstrated many causes for anemia are associated with RA, such as deficiencies of iron, vitamin B12, and folic acid, as well as decreased iron release from the mononuclear phagocyte system (MPS) and decreased absorption of iron ²¹. Increased apoptosis in the BM erythroid progenitor and precursor cell, these abnormalities were associated with a markedly increased local TNF production by patient BM stromal cells ⁹. TNF and IL-6 might be a mediator of impaired erythroid colony growth at stem cell level then inhibition erythropoiesis ²². The present study in agreement with ² who found most patients with RA has anemia that could cause reduction in hemoglobin level in RA, decreased survival of the RBCs. The results of present study revealed that the incidence of rheumatoid arthritis was 40% in (48-61) years for males and females infected with RA. Rheumatoid arthritis has been reported to decline with age may be: due to reduced survival of patients with RA, a prevalence of 3-4% being noted in the 65-74 years age group compared with a prevalence of 1.8-2.2% in those aged 75 years or older ²³.

Conclusions

dyslipidemia was observed in RA is a frequent occurrence and may be considered as a secondary impact of chronic inflammatory state seen in RA patients, also serious hematological abnormalities violations that can be caused by the activity of the disease were revealed.

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