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The Physiological Role of FAS and IL-17A as a Markers in the Diagnosis of Rheumatoid Arthritis

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ABSTRACT

Objective: The chronic autoimmune disease affecting the joints that are characterized by a progressive symmetric inflammation of affected joints resulting in cartilage destruction, bone erosion, and disability has been called Rheumatoid arthritis (RA). The aim of this study is to the assessment of FAS and lipid profiles in Iraqi patients with RA. Methods: In the current study, the demographic characteristics of the 90 studied subjects, 45 patients with RA, and 45 control subjects.

Results: The result showed statically significance for increased cholesterol, and LDL in the study group (p-value<0.0001,<0.001 respectively), while HDL was found to be significant decrease (p-value< 0.001) and non-significant for TG, VLDL (p-value 0.1,0.09 respectively). The current study concludes that there is a significant difference in the level of the fatty acid synthase FAS enzyme between the patients (0.93 ± 0.53) and control group (0.74 ± 0.45), p-value (0.001) where the patients group has a higher level of the fatty acid synthase than the control group. This study conducted that there is a significant difference in the level of the IL-17A levels (pg/ml) between the patients (166 ± 13) and control group (87 ± 5), p-value (0.001) where the patients group has a higher level of the IL-17A than the control group.

Conclusion: Assessment of both FAS and IL-17A may be given as an appropriate and useful method for diagnosis and following with patients with RA.

KEYWORDS: Rheumatoid arthritis; Fatty acid synthase; IL-17A; lipid profile; RF

ARTICLE DETAILS

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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease affecting the joints. It is characterized by a progressive symmetric inflammation of affected joints resulting in cartilage destruction, bone erosion, and disability (1). While initially only a few joints are affected, in later stages many joints are affected and extra articular symptoms are common (2). Clinically, the symptoms of RA significantly differ between early stage RA and insufficiently treated later stages of the disease. Early stage RA is characterized by generalized disease symptoms such as fatigue, flu-like feeling, swollen and tender joints, and morning stiffness; and is paralleled by elevated levels of C-reactive protein (CRP) and an increased erythrocyte sedimentation rate (ESR) (3). While the cause of RA is unknown, both genetic and environmental factors were shown to contribute to RA development (4). Risk factors for the development of RA were reported to include smoking, obesity, exposition to UV-light, sex hormones, drugs, changes in micro biome of the gut, mouth, and lung, periodontal disease, and infections (5-8). IL-17A produced by Th17 cells promotes both the production of the pro-inflammatory cytokines IL-6, IL-8, and GM-CSF from epithelial, endothelial, and fibroblastic cells and neutrophil recruitment (9), which leads to local inflammation and promotes disease progression. By these actions, IL-17A contributes to bone erosion, cartilage destruction, and neoangiogenesis in RA patients (10). In addition, IL-17A was shown to also promote matrix metalloproteinase (MMP)-1

production by synoviocytes, leading to cartilage destruction (11). Angiogenesis plays a critical role in the pathogenesis of RA. In this context, IL-17A was shown to enhance both endothelial cell migration (12) and the production of vascular endothelial growth factor (VEGF) by synovial fibroblasts (13). Fatty acid synthase (FAS) is an enzyme that in humans is encoded by the FASN gene (14). FAS is a multi-enzyme protein that catalyzes fatty acid synthesis. FAS is not a single enzyme but a whole enzymatic system composed of two identical 272 kDa multifunctional polypeptides, in which substrates are handed from one functional domain to the next (15). Its main function is to catalyze the synthesis of palmitate (C16:0, a long-chain saturated fatty acid) from acetyl-CoA and malonyl-CoA, in the presence of NADPH (16). The aim of this study to assessment of FAS, IL-17A and lipid profile in Iraqi patients with RA

METHODS

Measurement of Serum Lipid Profile:

Total cholesterol TC, triglyceride TG, high density lipoprotein HDL, low density lipoprotein LDL, and very low density lipoprotein VLDL were done by spectrophotometric methods depending on instructions of manufacture.

Measurement of Serum of fatty acid synthase FAS and IL-17A:

The Sandwich-ELISA was used to estimated FAS and IL-17A levels. The micro ELISA plate supplied in this package has been pre-coated with a Human FAS-specific antibody. The micro ELISA plate wells are added to standards or samples and mixed with the specific antibody. A biotinylated detection antibody specific to the conjugate of Human FAS and IL-17A and Avidin-Horseradish Peroxidase (HRP) is then successively added and incubated to each microplate. They wash away free components. Each well is applied to the substrate solution. Blue in color can appear only in certain wells containing Human FAS and IL-17A, biotinylated detection antibody, and Avidin-HRP conjugate. By applying the stop solution, the enzyme-substrate reaction is terminated and the color turns yellow. At a wavelength of 450 nm ± 2 nm, the optical density (OD) is measured spectrophotometrically. The OD value is proportional to the concentration of human FAS. The standard curves of FAS and IL-17A is showing in figure 1:

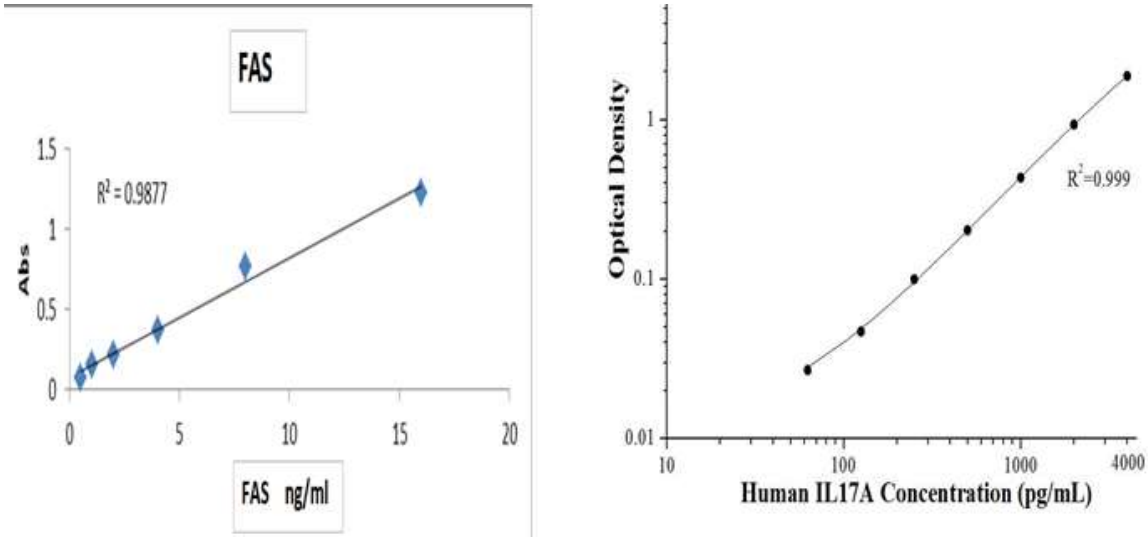

Figure 1: FAS and IL-17A standard curves

Statistical analysis

The statistical analysis of this prospective study performed with the statistical package for social sciences (SPSS) 20.0 and Microsoft Excel 2013. Independent sample t-test used for comparison between two groups while, ANOVA used for comparison among more than 2 groups. Categorical data were described as count and percentage. Chi-square test used to estimate the association between variables. The lower level of accepted statistically significant difference is bellow or equal to 0.05.

RESULTS

In the current study, Demographic characteristics of the 120 studied subjects, 60 patients with RA, and 60 control subjects, There were not statically significant differences in mean age, and BMI between the RA patients and control groups , most properly due proper matching between both groups as shown in table 1:

Table (1): Mean age and BMI of the studied subject

Characteristics	RA	CONT	P-value
Age (years)	49.5 ± 10.7	48.1 ± 19.6	0.322
BMI kg/m2	25.1 ± 2.9	25.9 ± 1.9	0.212

The table (2) show a higher incidence of RA in female (67%) in comprise to the male (33%):

Table (2): Distribution of Gender among RA and CONT groups.

Sex	Study groups		P-value
	RA patients	Control	
Female	40	30	0.576 NS
%	67%	50%	
Male	20	30	
%	33%	50%	
Total	45	45	

In the figure 2, which contain the percentage of the patients that has positive RF and patients that has negative RF, most of the patient (68%) has positive RF while the remaining (32%) has negative RF with the P-value < 0.05. The control group is subdivided into two subgroups the first have positive RF and consisting about 10 % of the control group and the remaining 90 % from the control group has negative RF

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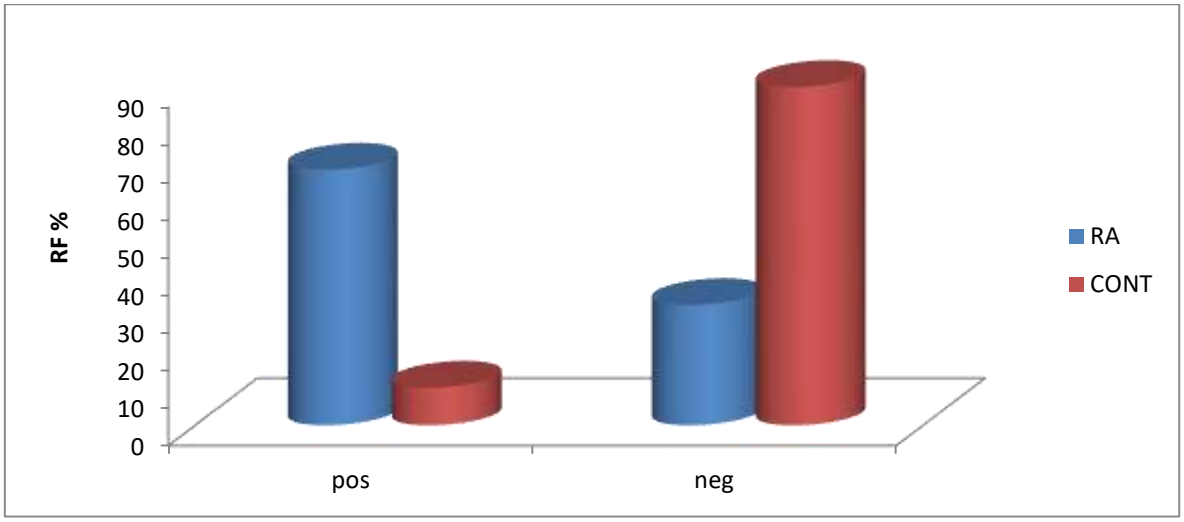

Figure (2): Percentage of RF in RA and CONT groups

Finding in the result statically significant for increase cholesterol, ,LDL in study group (p-value <0.001,<0.001 respectively) ,while HDL was found to be significant decrease (p-value< 0.001) and non-significant for TG,VLDL(p-value 0.1,0.09 respectively) show in table(3):

Table (3): TC, TG, VLDL, LDL, and HDL level

PARAMETER	RA patients		Control		P-value
	Mean	SD	Mean	SD	
TC (mg/dl)	169.14	34.21	149.22	21.57	<0.001**

TG (mg/dl)	149.33	34.26	150.11	27.11	0.212 NS
HDL (mg/dl)	35.55	6.33	44.09	8.33	<0.001**
LDL (mg/dl)	109.08	30.02	71.09	26.04	<0.001**
VLDL (mg/dl)	29.21	7.09	31.09	4.99	0.054NS

In the figures 3 and 4, the current study concludes that there is a significant difference in the level of the FAS and IL-17A between the patients (1.53 ± 0.48) and control group (0.69 ± 0.13), p-value (0.001) where the patients group has a higher level of the FAS and IL-17A than the control group.

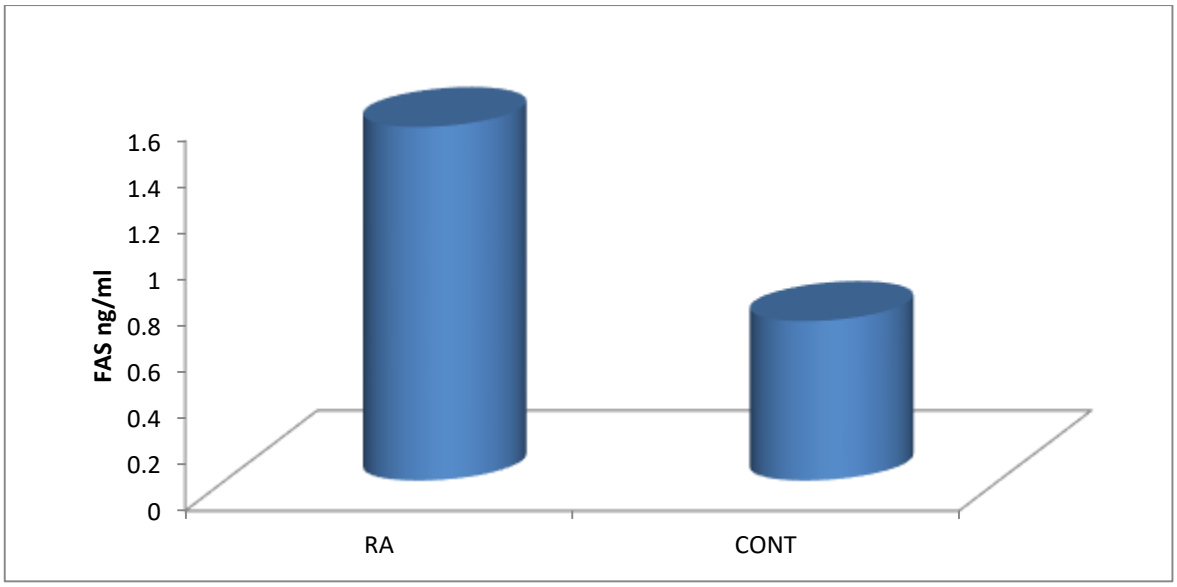

Figure (3): FAS (ng/ml) levels in the RA group and CONT group

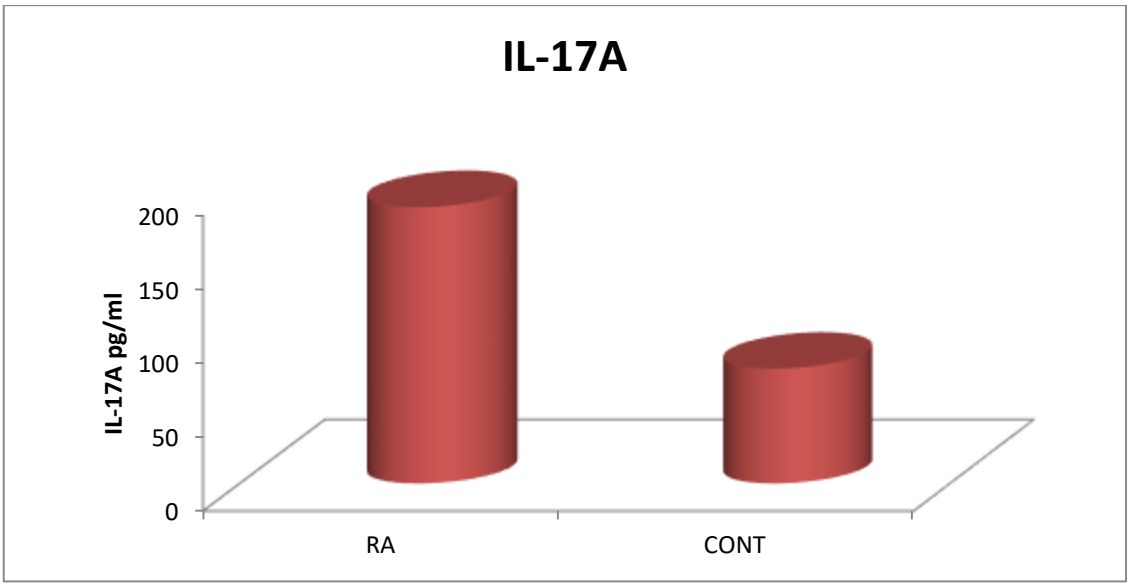

Figure (4): IL-17A (pg/ml) levels in the RA group and CONT group

DISCUSSION

RA is an inflammatory progressive disease which in the absence of appropriate treatment that can lead to joint destruction and prognosis of RA may be predicted based on the presence of some clinical and laboratory evidences and the new criteria for classification of RA provide opportunity for earlier treatment (17). A patient with inflammatory arthritis may pass several stages from the onset of arthritis to a specific form of rheumatic diseases such as RA (18). This study aimed to investigation the role of FAS and IL-17A as a prognostic indicator in the diagnosis of RA. From the results of study concludes that there is a significant difference in the

level of the FAS and IL-17A between the patients (1.53 ± 0.48) and control group (0.69 ± 0.13), p-value (0.001) where the patients group has a higher level of the FAS and IL-17A than the control group. Tański et al. (19) were reported that fatty acids has an essential component in the synthesis of eicosanoids that exhibit anti-inflammatory properties and due to the documented positive influence of unsaturated fatty acids on treatment outcomes, the use of a diet rich in long-chain unsaturated fatty acids should be the standard of care, along with pharmacotherapy, in the treatment of RA patients. Many studies suggested that the use of an anti-inflammatory diet containing fish oil significantly reduces the number of tender and swollen joints and duration of morning stiffness of RA patients (20-24). In the study by Galarraga et al. (25) of 49 patients, 19 (39%) in the cod liver oil group and five (10%) in the placebo group were able to reduce their daily NSAID requirements by >30%. From the above truths found were no differences between the groups in the clinical parameters of RA disease activity or in the observed side effects. The results of this work found the statically significant for increase cholesterol, ,LDL in study group (p-value <0.001,<0.001 respectively) ,while HDL was found to be significant decrease (p-value< 0.001) and non-significant for TG,VLDL (p-value 0.1,0.09 respectively). In a study by Fraser et al. (26) found that changes in fatty acids after a seven day fast in rheumatoid arthritis (RA) patients will inhibit T-lymphocyte proliferation in vitro and it was demonstrated that both the concentration of the FFA mixture and the ratio of unsaturated and saturated fatty acids significantly affected lymphocyte proliferation in vitro (p-value < 0.0001). Robert and Miossec (27) were found that IL-17 is a new tools and concepts are required to identify patients that could benefit from these IL-17 targeted therapies in RA and the development of predictive biomarkers of response has started with the emergence of various bioassays . In conclusion, the assessment of FAS and IL-17 may be useful to diagnosis and following up patients with RA.

CONCLUSION

The combination between FAS and IL-17A with lipid profile suggested a new approach for diagnosis and following up of patients with RA.

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CONFLECT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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