ASSESSMENT OF FATTY ACID SYNTHASE AND ITS CORRELATION WITH LIPID PROFILE IN IRAQI PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract

Objective: RA is a systemic illness, in addition to articular involvement, extra-articular manifestations like ocular, skin, cardiac, pulmonary, neurological can occur. The actual mechanism causes an invasion of joints by the immune system. These responses to the immune system cause inflammation and spread of the joint capsule and also affect cartilage and bone. The aim of this study to assessment of FAS and lipid profile in Iraqi patients with RA. Methods: In the current study, Demographic characteristics of the 90 studied subjects, 45 patients with RA, and 45 control subjects. Results: The result showing 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). The current study concludes that there is a significant difference in the level of the fatty acid synthase 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. Conclusion: Assessment of FAS and lipid profile may be useful in diagnosis and following of patients with RA.

Keywords: Rheumatoid arthritis, Fatty acid synthase, lipid profile, RF

I. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that mainly affects the synovial joints and contributes to repeated inflammations of the membrane of the Synovial, ultimately leading to the destruction of the joints, deformity, and disability [1]. RA is a systemic illness, in addition to articular involvement, extra-articular manifestations like ocular, skin, cardiac, pulmonary, neurological can occur. The actual mechanism causes an invasion of joints by the immune system. These responses to the immune system cause inflammation and spread of the joint capsule and also affect cartilage and bone [2]. Although the etiology of RA has not yet been thoroughly established, a combination of genetic and environmental factors as well as many other autoimmune-initiating agents are thought to have been involved [3]. A joint is a point where two bones make contact. Joints can be classified either histologically on the dominant type of connective tissue for example (fibrous, cartilaginous, and synovial), functionally based on the amount of movement permitted, for example, synarthrosis (immovable), amphiarthrosis (slightly moveable), and diarthrosis (freely moveable) [4]. To allow mobility and flexibility of the body, a joint is where two bones meeting producing fluid. This lining is very thin in a healthy joint, has very few blood vessels in it, and contains no white blood cells. The immune system typically assaults the synovium first in rheumatoid arthritis [5]. White blood cells pass and enter the synovium from the bloodstream, and small blood vessels penetrate the area. The synovial membrane, therefore, becomes dense and inflamed, leading to unwanted tissue formation. Inflammation also includes the release of different biochemical substances that cause discomfort, swelling, and damage to the joints. The underlying cartilage, bone, ligaments, and tendons also may be affected by such substances. These compounds may also trigger fatigue and a general feeling of being unwell as they reach the bloodstream. The joint loses its form and orientation gradually and undergoes changes that are often irreversible [6]. Synovium in rheumatoid arthritis is invaded by the interaction of T and B cells, causing the activation of cytokine-producing T cells and the activation of autoantibodies, including RF and ACPA, by B cells. TNF and interferon-gamma (IFN-γ), produced by T cells, are activated by Synovial macrophages. Several pro-inflammatory cytokines, including (TNF, IL-1, and IL-6), which act on synovial fibroblasts to generate additional cytokines, are released by macrophages, forming a positive feedback loop. Synovial fibroblasts proliferate, inducing synovial
hypertrophy and developing matrix metalloproteinase and proteinases that weaken cartilage and soft tissues [7]. Since triglycerides may not accumulate in foam cells, the correlation between plasma triglycerides and cardiovascular atherosclerotic disease (ASCVD) may be triggered by the remaining lipoproteins. The residues will accumulate in the lining of the arteries, where macrophages can be ingested, facilitating the formation of foam cells and, eventually, the formation of a fatty line that leads to plaque growth [8]. Hypertriglyceridemia is often associated with higher concentrations (which may be more atherogenic than other LDL particles) of small dense LDL particles, decreased HDL particles. The aim of this study to assessment of FAS and lipid profile in Iraqi patients with RA.

II. METHODS

Measurement of Serum Lipid Profile and RF:
Rheumatoid factor RF, 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:
The Sandwich-ELISA was used to estimated FAS 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 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, 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. standard curve of FAS is showing in figure 1:

![FAS standard curve](image)

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.

Ethical issue
This study was performed depending on ethical instructions of the department of community medicine /college of medicine/ Babylon university. The approval was taken from all subjects whom participate in this study.

**III. RESULTS**

In the current study, Demographic characteristics of the 90 studied subjects, 45 patients with RA, and 45 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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RA group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.8 ± 11.8</td>
<td>47.1 ± 10.5</td>
<td>0.48</td>
</tr>
<tr>
<td>BMI kg/m2</td>
<td>24.6 ± 3.4</td>
<td>25.7 ± 2.6</td>
<td>0.14</td>
</tr>
</tbody>
</table>

The table (2) show a higher incidence of RA in female (84.4%) in comprise to the male (15.6%):

Table (2): Distribution of Gender among RA and control group.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Study groups</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA patients</td>
<td>Control</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>%</td>
<td>84.4%</td>
<td>82.2%</td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>%</td>
<td>15.6%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
<td>45</td>
</tr>
</tbody>
</table>

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 (60%) has positive RF while the remaining (40%) 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 4.4% of the control group and the remaining 95.6% from the control group has negative RF.
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

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>RA patients</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>170.22</td>
<td>37.61</td>
<td>148.38</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>142.76</td>
<td>34.26</td>
<td>149.93</td>
</tr>
<tr>
<td>High-density lipoproteins (mg/dl)</td>
<td>36.64</td>
<td>7.28</td>
<td>41.98</td>
</tr>
<tr>
<td>Low-density lipoproteins (mg/dl)</td>
<td>104.96</td>
<td>31.92</td>
<td>78.07</td>
</tr>
<tr>
<td>very Low-density lipoproteins (mg/dl)</td>
<td>28.47</td>
<td>6.83</td>
<td>30.04</td>
</tr>
</tbody>
</table>

In the figure (3), the current study concludes that there is a significant difference in the level of the fatty acid synthase 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.
IV. DISCUSSION

The higher percent of the patient with positive RF than the patients with negative RF are attributed to this are considered autoantibodies are pentamer IgM antibodies that bind to the Fc portion of human immunoglobulin G which making it elevated at an autoimmune disease or inflammation, as well as in healthy patients, and because of the RA are inflammatory disease so these would result in the elevation of this protein [9]. Rheumatoid factors (RF) are found in a variety of diseases, including autoimmune and non-autoimmune diseases, in addition to rheumatoid arthritis (RA). Up to 4% of young, healthy people and the elderly have been shown to have them[10]. The sensitivity of the IgG rheumatoid factor test is 60 percent, according to our findings. The findings of this study agree with those of a previous study that found IgG rheumatoid factor sensitivity to be in the 60–80 percent range Dessie et al.[11]. Dyslipidemia was commonly found in Rheumatoid Arthritis, which may be the cause of this abnormality in lipid levels in the RA community. This may be seen as a side effect of the persistent inflammatory state seen in RA. Lipid irregularities increased the risk of cardiovascular disease[12]. The main factor which causes dyslipidemia among the RA patients is different such as genetic factor, disease activity, drugs and pain which results in the reduction in the physical activity of the patients[13]. In the table (3) there is an abnormality in the level of the lipid profile which is characterized by the increasing the level of the LDL and cholesterol in the patient's group than the control group while there is a reduction in the level of the HDL in patients group than control group this result agreement with consistent study Kumar et al[14]. The Elevated level of LDL and cholesterol are attributed to the drugs that are ingested by the patients for the treatment of the disease. RA characterized by the elevation of the level of the inflammatory cytokines such as IL-6 and TNF and these cytokines can increase the expression of the pf the receptors for the LDL and the SR-B1 receptors which can increase the hepatic absorption and biliary excretion of the LDL causing the reduction in the level of the LDL, after ingestion the treatment of the RA which has the ability for blocking the IL-6 and TNF from binding to its receptors, the expression of the LDL receptors and SR-B1 receptors were decreases which causing the elevation of the LDL and cholesterol [15,16]. RA is characterized by increasing the inflammatory response and this inflammation resulted in the decreasing the cholesterol efflux capacity of the HDL which resulting in the decreasing the function of the HDL for transferring the cholesterol from the tissue to the liver [17]. Inflammation in RA also increases CETP activity, which is involved in HDL metabolism and leads to a decrease in HDL-C levels[18]. Due to the increasing inflammation which causing the increasing the releasing of the free radicals causing the oxidizing of the LDL and formation of the oxidized LDL which resulting in the precipitation of the LDL causing the narrowing of the arteries and resulting in arteriosclerosis and cardiac disease Tsoupras et al;[19]. According to the result of the current study, the patients with RA are more prone to cardiac disease than the control group due to the inflammation that occurs in patients of RA than the normal subjects Toosi et al. [20]. In the current study show increase in the level of TC, LDL, and low in HDL in RA group, according to the result, considerable risk factor CVD is more prevalent in RA patients than the normal population, this agrees with previous study [21]. A previous study showing has been shown to affect inflammation to altered metabolism and de novo FAS are essential for CD4+ and CD8+ T cell effector fates. FAS is a protein that catalyzes the de novo synthesis of fatty acids, produces fatty acids that can be used for energy storage, membrane assembly and repair, and secretion in the form of lipoprotein triglycerides. Excess FAS are converted to triglycerides and deposited as lipid droplets or secreted as very low-density lipoproteins [22].
V. CONCLUSION

Assessment of FAS and lipid profile may be useful in diagnosis and following of patients with RA.

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Nil

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CONFLICT OF INTEREST

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

REFERENCES