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THE LEVEL OF SERUM ADIPONECTIN AND ITS POSSIBLE ROLE IN RHEUMATOID ARTHRITIS PATIENTS

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Abstract:

Introduction:

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that damages joints and impairs daily life for those affected. RA is caused on by three risk factors: genetics, gender, and smoking. Factors such as pro-inflammatory chemicals, insulin resistance, total oxidant status, adhesion molecules and the use of corticosteroids in chronic inflammatory disorders also contribute to the acceleration of atherosclerosis. Adipose tissue plays an important role in maintaining overall body balance. There are numerous bioactive peptides known as adipo(cyto)kines secreted by adipocytes. Adiponectin, the most common adipokine produced by adipose tissue, has anti-atherogenic properties. Adiponectin has 244 amino acids and is an abundant protein hormone. Recent study suggests that adiponectin may be useful in the diagnosis of RA and other rheumatic diseases.

Methods:

The research included 70 RA patients (25 men and 45 women) ranging in age from 45 to 65, as well as 30 healthy individuals (ten men and twenty women) ages 40 to 70. All individuals had their demographic and biochemical profiles and serum adiponectin concentrations analyzed.

Results:

Our results showed that Adiponectin serum levels were significantly lower in the Rheumatoid arthritis group compared with healthy individuals. Adiponectin had moderate positive correlations with rheumatoid factor (RF).

Conclusion:

The variations in adipokine levels that we observed could play a role in the diagnose of Rheumatoid Arthritis.

Keyword: Rheumatoid arthritis, Adiponectin, Adipokines, Rheumatoid factor.

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Introduction:

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease that damages joints and impairs daily life for those affected. RA is caused on by three risk factors: genetics, gender, and smoking.[1]One to two percent of the world's population has rheumatoid arthritis (RA). When compared to the general population, those with RA have a higher chance of dying young. Patients with RA are more likely to die early than the general population because of cardiovascular disease [2]. The increased cardiovascular risk in chronic inflammatory disorders is only partially explained by Framingham risk factors. Factors such as pro-inflammatory chemicals, insulin resistance, total oxidant status, adhesion molecules and the use of corticosteroids in chronic inflammatory disorders also contribute to the acceleration of atherosclerosis. [3]

It's not only a place to store fat; adipose tissue plays an important role in maintaining overall body balance. There are numerous bioactive peptides known as adipo(cyto)kines secreted by adipocytes. There are many different physiological and pathological processes that these peptides are involved with include atherosclerosis, insulin resistance, inflammation, and immunology. These peptides include tumor necrosis factor (TNF), leptin, and resistin .[4]

Adiponectin, the most common adipokine produced by adipose tissue, has anti-atherogenic properties. Adiponectin has 244 amino acids and is an abundant protein hormone. Collagens VIII and X and complement component C1q have a similar structure to this one. There are three primary cell types that express this protein: adipocytes, myocytes, and endothelial cells [4]. adiponectin is a human hormone that is encoded by a gene on chromosome 3q27 Adiponectin has three receptors: AdipoR1, Adipo R2, and Tcadherin, the first of which is more abundantly expressed in skeletal muscle, the second in the liver, and the third in the heart and arteries[5]. An anti-diabetic, anti-atherogenic, and anti-inflammatory hormone produced by adipose tissue is adiponectin [6]. The preventive effect of adiponectin in vascular disease has been well-documented, but recent research suggests that it may operate as a proinflammatory factor in joints, where it may be implicated in matrix breakdown. Furthermore, these variations in adiponectin's activities are connected to the protein's oligomerization level and opposing actions have been documented for both low and high molecular weight isoforms [7]. Adiponectin has been linked to RA pathogenesis in several studies, according to the literature. According to the findings, adiponectin can trigger the production of VEGF and MMPs-1 -13 in fibroblast-like synoviocytes (FLSs), resulting in joint inflammation and destruction [8]. According to Giles and colleagues' cross-sectional study, adiponectin levels are linked to radiographic damage in RA patients, suggesting that this adipokine may be a mediator of the paradoxical relationship between increasing adiposity and radiographic damage protection in RA. This is because adiponectin levels in the blood fall as weight increases. When you take this into account, adiponectin may be a key mediator in the link between growing obesity and radiographic damage seen in Rheumatoid Arthritis research [9].

Adiponectin may play a role in the diagnosis of RA and other rheumatic diseases, according to recent research. Although the function of adiponectin is still not fully understood, research has shown that it has both pro-inflammatory and anti-inflammatory characteristics. The degree of oligomerization of the

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protein appears to be a factor in the apparent differences in adiponectin's various activities and in the activation of particular signaling cascades. High- and low-molecular-weight isoforms have been shown to have opposing effects.[10]

The erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF) are positively correlated with increased adiponectin levels. Anti-TNF agents (e.g. infliximab and etanercept) have been shown to enhance total and high molecular weight adiponectin in RA patients .[11] Because this adipokine has such negative effects on joint inflammation, it has been suggested that adiponectin be used as a possible therapeutic target for blocking therapies[12].

The aim of this study was to evaluate RA patients' serum levels of adiponectin to those of healthy controls.

Materials and Methods

Study participants

The current study took place between October 2020 and March 2021 at Al-Baghdad teaching hospital. The current study included 70 RA patients (25 men and 45 females) and a control group of 30 healthy individuals (10 males and 20 females). Patients with rheumatoid arthritis ranged in age from 45 to 65 years, whereas the control group ranged in age from 40 to 70 years. The Department of Chemistry, College of Science, Al-Nahrain University, Baghdad, and the Iraqi Ministry of Health's Research Ethics Committee approved this study.

Exclusion criteria included a history of hypertension, heart failure, diabetes mellitus, hypothyroidism, smoking and hepatic or renal problems, as well as individuals taking any medication.

Patients and healthy individuals supplied 7 milliliters of venous blood. The blood was divided into two tubes: three milliliters went into ethylene diamine tetra acetic acid (EDTA) tubes for determining the Erythrocyte Sedimentation Rate (ESR), and five milliliters went into gel tubes for 15 minutes to coagulate. Centrifugation at 1840 x g for 15 minutes at room temperature was used to separate serum from blood samples. Aliquots of serum were isolated and stored at -70°C until testing.

Biochemical Analysis

The serum levels of adiponectin were measured using enzyme linked immune-sorbent assay (ELISA) provided by (MyBioSource, USA). The fluorescence Immunoassay (FIA) method was used to evaluate the RF levels(ichroma,Korea).

Measurement of Body Mass Index (BMI)

BMI was measured by dividing weight (in Kilograms, Kg) by height squared (in meter, m) for each participant.

Statistical Analysis

The present study used GraphPad Prism 8.0.2 to collect demographic and biochemical data (San Diego, California, USA). The unpaired t-test was used to determine the mean standard deviation (STD) and

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significant differences (P-value) between the means of the two groups investigated. Pearson's correlation coefficient was used to evaluate correlations between parameters in this investigation. P 0.05 was judged significant statistically.

Result:

Table 1 summarizes the demographic characteristics of the two groups investigated (Rheumatoid arthritis, and control). The preliminary analysis revealed that There were no significant differences in age or gender between the RA and control groups (p=0.5565), however there were significant variations in BMI between the RA and control groups (p =0.0993). Our data suggest that there were statistically significant variations in RF (p= 0.0001).

The difference in adipokine concentrations between the two groups is seen in Table 1. Serum adiponectin levels were substantially lower (p <0.0001) in the RA group than in the control group, according to statistical analysis.

Pearson's correlation coefficient was calculated between the study's various variables. Significant associations between adiponectin and RF were seen in the RA group (r=0.283, P=0.026).

Parameter	Control	RA	P-Value	Significant
Age(year)	53.39±8.2	54.53±6.9	0.5565	NS
Gender(male\female)	10\20	35\45	—	—
BMI	29.6 ± 2.4	30.2 ± 3.4	0.0993	NS
RF(IU\Ml)	15.95±1.771	63.40±34.61	<0.0001****	HS
ADP (ng/mL)	80.5 ± 5.6	67.7 ± 10.7	<0.0001****	HS

Discussion:

In our study, we focused on one of the adipokines known as adiponectin and found that the levels of total adiponectin were lower in patients with RA than those in the healthy individuals. Moreover, we also found that in the serum of patients with RA, total APN was positively associated with RF levels.

In the current study, the RA patients were obese (30.2 ± 3.4),the marked inflammation encountered in RF(63.40±34.61)this agreed with Jonsson et la[13]who reported that RA patients explained this finding by the increase in inflammatory cytokine production.

In this study, we found adiponectin levels in RA patients are significantly lower (P value<0.0001) compared to controls, As shown in figure (1). Similar to our findings, El Hini et al. [14] and Li et al. [15]have reported higher adiponectin levels in healthy controls compared to RA patients, and against that Rho et al. [16] and Lee and Bae et al who concluded that concentrations of adiponectin are increased in patients with RA. [17]

The results of our study may just suggest that the actual relationship of adiponectin with inflammatory milieu of RA is quite complex. Physiologically, adiponectin increases the production of anti-

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inflammatory cytokines from activated inflammatory cells and inhibits the release of pro-inflammatory cytokines. Conversely, pro-inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and IL-6 are known to suppress adiponectin production. Some experimental studies have demonstrated that the association of adiponectin with TNF-α is bidirectional and inverse.[18]Studies have shown that anti-TNF-α treatment results in increased adiponectin levels. Other reasons why adiponectin concentrations have shown variable results between studies include variable disease duration, disease activity, sample size, and ethnicity of the study population. [18]

Our study showed the serum adiponectin of RA patients were not related to age and body mass index similar to Senolt et al. [19] The discrepancy in the results of different research is most likely due to differences in the methods utilized to assess adiponectin, genetics, and race.

There is a positive correlation between ADP and rheumatoid factor (RF) levels [20].As is well known, RF is the disease-defining antibody in rheumatoid arthritis [21]. In rheumatoid arthritis patients, antibodies such as RF and anti-CCP antibodies are induced by activated B cells in response to antigens given to T cells [22]. As demonstrated in this study, serum APN levels were favorably linked with serum RF levels. We can hypothesize that APN may also play a role in antigen presentation, or that it may function as a protective factor against RF.

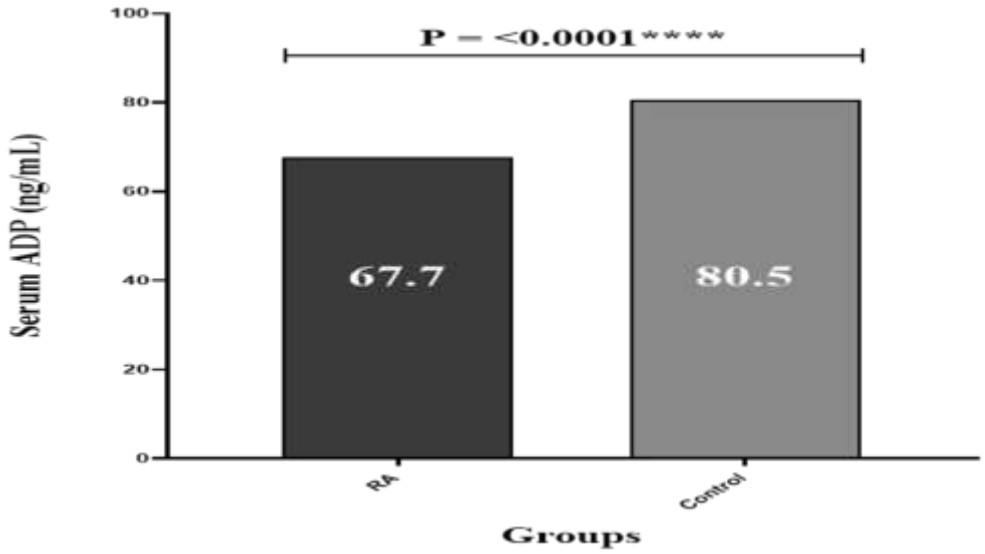

Figure (1): Mean Serum ADP in RA and Control.

In conclusion, our findings reveal that adiponectin levels are significantly lower. Therefore, these alterations in adiponectin levels may play a key role in the development of RA-related inflammation.

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