Measurement of Anti-Cyclic Citrullinated Peptide, Leptin Hormone, and Lipoprotein (a) In Iraqi Female Patients with Rheumatoid Arthritis

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Summary:

Back ground:- Rheumatoid arthritis is one of the most common forms of inflammatory polyarthritis, with a prevalence of approximately 0.8% of adults worldwide, Rheumatoid arthritis patients may become disabled within few years if untreated that may lead to permanent disability. Different biomarkers have been assessed for the improved diagnosis of Rheumatoid arthritis, including a wide range of autoantibodies. However, only rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACCP) have gained wide acceptance.
Aim of the study to investigate the levels of ACCP, Leptin, and Lipoprotein (a) in females with RA to provide information on possible pathophysiologic mechanisms, and to give recommendations for determination of these parameters in diagnosis and follow up of Rheumatoid arthritis patients.
Patients and methods:- The study included Forty women with RA and Thirty apparently healthy women with matching age and weight as controls.The patients were selected at the outpatient clinic of Rheumatology & Rehabilitation in Medical City/ Baghdad Teaching Hospital during the period from (May2013) to (December2013).
Results:-The results showed that levels of ACCP antibodies in serum of patients with RA were significantly higher than in serum of healthy control. Also there were significant differences between mean of serum leptin level and Lp (a) in patients compared to the control group.
Conclusion:- Serum biomarkers like ACCP, Leptin, & Lipoprotein (a) assays are becoming increasingly available and may help in early diagnosis and assessment of complications in Rheumatoid arthritis patients.
Kew word:- ACCP, Leptin, lipoprotein, RA.

Introduction:

Rheumatoid arthritis (RA), (the most common form of inflammatory polyarthriti) is prevalent in approximately 0.8% of adults worldwide, if untreated, 20%–30% of RA patients become so severely disabled within few years following initial diagnosis that they become permanently crippled [1]. Various serum biomarkers have been assessed to improve diagnosis and prognosis of RA, including a wide range of autoantibodies. However, only rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACCP) have gained wide acceptance [2]. Adipose tissue is a major source of several mediators termed adipocytokines that include leptin, which is best known for its ability to regulate body weight by decreasing food intake and increasing energy expenditure, also has immunomodulatory effects. However, information regarding its relationship with inflammation and disease activity in RA is conflicting [3,4]. Lipoprotein (a): Lp(a) is an important risk factor for premature atherosclerosis in autoimmune diseases [5]. Lp(a) was associated with elevated CRP-level and erythrocyte sedimentation rate (ESR) and therefore playing an important role in the acute phase cascade reaction process in RA

patients] 6]. Coronary atherosclerosis and acute myocardial infarction are the most common causes of death in patients with RA [5,6].The aim of this study is to investigate the levels of ACCP, Leptin, and Lp (a) in females with RA to provide information on possible pathophysiologic mechanisms, and to give recommendations for determination of these parameters in diagnosis and follow up of RA patients.

Patients and Methods:

The study included 70 women divided into two groups:
1. Forty female patients with RA.
2. Thirty apparently healthy females with matching age and weight as controls.
The patients were selected at the outpatient clinic of Rheumatology & Rehabilitation in Medical City/ Baghdad Teaching Hospital during the period from (May 2013) to (December 2013) Both groups were in the postmenopausal period and did not receive hormonal replacement therapy. Exclusion criteria included diseases that might have some influence on measured parameters such as thyroid disorders, other endocrinopathy, renal insufficiency, heart failure, arterial hypertension, diabetes mellitus, hyperlipidemia, neoplastic

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disease or mental disease, and cigarette smoking. Blood was withdrawn from all studied women; centrifuged to obtain serum, and measurements of ACCP, leptin, and Lp (a) were done by ELISA technique using kits provided by HUMAN company/Germany.

Statistical analysis:

Results were expressed as mean ± standard deviation (SD). Student`s t-test was used; p value< 0.05 was considered statistically significant.

Results:-

The results showed that levels of ACCP antibodies in serum of patients with RA was significantly higher than levels in serum of healthy control group (p<0.05). Also there were significant differences between mean of serum leptin level and Lp (a) level in patients compared to the control group (p <0.05), as shown in table (1).

Table1: Levels of ACCP, leptin, lipoprotein A in serum of the study groups

parameter	patients(n=40) mean±SD	control(n=30) mean±SD	P value
ACCP(μ/ml)	29.7±0.765	9.8±0.881	<0.05
Leptin(ng/ml)	25.9±4.5	14.8±6.2	<0.05
Lipoprotein (a) (mg/dl)	39.2±20.6	14.8±9.7	<0.05

Discussion:

Rheumatoid arthritis (RA) is an autoimmune disease affecting ~1 % of the population [7]. Although major advances have been made in the treatment of RA, relatively little is known about disease pathogenesis. Autoantibodies, present in approximately 60 % of the patients with early disease, might provide indications for immunological mechanisms underlying RA [8]. Among the RA-associated autoantibodies, especially anti-citrullinated protein antibodies (ACCPs) have been studied intensively in the last decade [7].The current study showed a difference in ACCP levels between patients and controls which agree with previous studies [9-13]. The discovery of ACCP resulted into novel insight in RA pathogenesis and allowed division of the heterogeneous entity of RA into an ACCP-positive and ACCP-negative subset of disease [10-14]. Since ACCP are present before the onset of RA symptoms and are predictive of RA development, they are a valuable diagnostic test early in the course of the disease. Also antibodies activating the enzyme involved in citrullination, might contribute in collaboration with ACCP to aggravate erosive outcome of the disease [14]. Data indicate that ACCP has a higher specificity than Rheumatoid Factor for early RA, good predictive validity, high sensitivity, apparent cost-effectiveness and good stability and reproducibility [11]. RA is a chronic inflammatory disease associated with dyslipidemia and cardiovascular complications [5]. This study showed that patients with RA had higher levels of serum leptin; which agrees with previous studies [3-5,15-18]. TNF-α is one of the main proinflammatory cytokines

that plays a key role in pathogenesis of rheumatoid arthritis [16]. It has been shown that TNF-α increases secretion of leptin, as known as ob protein, hormone produced mainly by adipocytes. Also it has been suggested that cytokine-dependent hyperleptinaemia may be a potential cause of body mass reduction in patients with RA [17]. Elevated Lp(a) is an important risk factor for premature atherosclerosis and high Lp(a) levels are also associated with autoimmune diseases [19]. The current study revealed increased levels of Lp (a) in RA patients compared to control; which agrees with previous studies [5,6,19-21] . Dyslipoproteinemia observed in RA is proved to be associated with inflammation. On the other hand; inflammation in RA may cause changes in lipids and Lp (a) metabolisms[19]. Lp (a) contains a LDL-like particle with apolipoprotein B-100 linked to apolipoprotein(a) [20]. There is evidence that serum Lp(a) and LDL can act additively in the development of coronary heart disease. Lp (a) undergoes oxidative modification like oxidized LDL [21] and provokes an immune response [6,21]. This was supported by studies that found antibodies against oxidized-LDL and oxidized-Lp(a) being more prevalent in patients with specific autoimmune diseases like RA [21,22].

Coclusion:

ACCP assays are becoming increasingly available and less expensive especially in patients presenting with undifferentiated arthritis since it will help saving indirect costs of delayed diagnosis. Postmenopausal female patients with RA might have an independent adiposity-driven hyperleptinemia that is associated with the chronic inflammatory state of the disease. The measurement of Lp(a) levels in patients with autoimmune disease like RA might be an additional tool to identify patients at high risk for cardiovascular complications.

Author contributions:

Zina H. Abdul-Qahar :blood collection.
Halla G. Mahmood : statistical analysis.
Manal k. Rasheed : writing the research.

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