

LEPTIN /ADIPONECTIN RATIO A RISK FACTOR FOR CARDIOVASCULAR DISEASE IN EARLY RHEUMATOID ARTHRITIS WOMEN

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ABSTRACT : Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with pro-atherogenic changes by alters the function of adipose tissues; vascular endothelium and skeletal muscle these changes increase dyslipidemia, oxidative activity. The high prevalence of traditional cardiovascular risk factors and the systemic inflammatory process play a role in this pathogenesis. The present study was aimed to examine the leptin/ adiponectin ratio could serve as a predictable marker for cardiovascular disease in middle age women with early RA.

The comparative study included sixty-five women with a new diagnosis of RA attending to the department of rheumatology in Baghdad teaching hospital from and 40 healthy subjects as a control group. To all participant measuring RF, anti-CCP, leptin; adiponectin; hs-CRP and lipid profile were done also calculated atherogenic index of plasma (AIP).

The results indicated that serum leptin; adiponectin levels and leptin/adiponectin ratio were significantly higher in the RA group as compared to age matched control group in addition CRP, anti-CCP and RF were higher significant in patients group. Negative significant correlation founded between leptin/adiponectin ratio and CRP; RF; anti-ccp also between AIP and RF; anti-ccp. On the other hands, a positive significant correlation was found between AIP and leptin/adiponectin ratio; leptin; adiponectin and CRP.

The patients with RA are possible under risk to cardiovascular disease. Therefore, leptin/ adiponectin ratio considered as a marker for CVD in RA patients these finding suggest that patients with early RA exhibit raise leptin/ adiponectin ratio may be prone to cardiovascular disease.

Key words : Rheumatoid arthritis, cardiovascular risk factors, leptin, adiponectin.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with pro-atherogenic changes by alters the function of adipose tissues; vascular endothelium and skeletal muscle these changes increase dyslipidemia, oxidative activity, insulin resistance and endothelial dysfunction (Meune *et al*, 2009). RA accelerated coronary and extra coronary atherosclerosis that leads to a high risk of the development of cardiovascular. Actually, the detailed mechanisms involved in the pathogenesis of RA are still obscured and the pathogenesis has not been clearly defined. The high prevalence of traditional cardiovascular risk factors and the systemic inflammatory process play a role in this pathogenesis (Manzi and Wasko, 2000).

Adipocytokines are proteins secreted by white adipose tissue, among which leptin and adiponectin have been associated with regulatory functions on energy metabolism and mediating immune responses (Krysiak

et al, 2012). Previous studies claimed that both the production and effects of adipokines altered in autoimmune diseases including RA (Klein-Wieringa *et al*, 2011). Leptin belongs to the class I cytokine superfamily, consisting of a bundle of four α -helices. The level of leptin mainly produced by adipocytes and in several tissues including cardiovascular system such as blood vessels and cardiomyocyte (Raucci, 2013), but the circulating levels are correlated with white adipose tissue mass and its synthesis is regulated by inflammatory mediators (Kang *et al*, 2017). Adiponectin produced mainly by white adipose tissue and has a protective role for cardiovascular system by inhibits the production of endothelial cell and regulate many of atherogenic process steps such as angiogenic effects on the vasculature and antiapoptotic actions on endothelial cells, additionally adiponectin has anti-inflammatory actions (Kopp *et al*, 2005). In cellular studies, adiponectin was shown to increase gene expression and protein synthesis of many pro-

inflammatory and pro-destructive molecules that participate in the pathophysiology of RA (Otero *et al*, 2006). Also, adiponectin in joints acts as a pro-inflammatory factor and circulating levels correlate with severity of RA (Neumann *et al*, 2016).

So that the present study was aimed to examine the leptin/ adiponectin ratio could serve as a predictable marker for cardiovascular disease in middle age women with early RA.

MATERIALS AND METHODS

Study population

Sixty-five women with a new diagnosis of RA, who fulfilled the 2010 American College of Rheumatology, European League Against Rheumatism classification criteria for RA (Aletaha *et al*, 2010) attending to the department of rheumatology in Baghdad teaching hospital from October to December 2017 and 40 healthy subjects as a control group. Excluded any women take hyperlipidemia drugs smoking, diabetes mellitus; thyroid disorder; hypertension, renal and liver disorder, cardiac disease.

Biochemical measures

Blood was drawn to measure rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (anti-CCP), leptin; adiponectin and high sensitivity C-reactive protein (hs-CRP) concentrations were determined by using enzyme-linked immune sorbent assay (ELISA) method (Engvall and Perlmann, 1979). Other measurements: total cholesterol (TC) (Richmond, 1974), triglyceride (TG) (Fossati and Prencipe, 1982), high density lipoprotein (HDL) (Burstein *et al*, 1970). Also, calculated atherogenic index of plasma (AIP) was done from the formula $[\log(TG/HDL-c)]$ (Ikewuchi and Ikewuchi, 2009).

Statistical analysis

Data were assessed using the software SPSS v22.0 (SPSS Inc., Chicago, IL, USA). Variables are reported as mean \pm standard deviation (SD).

Variables were compared by using the Student's t-test. Correlation analyses were analyzed with Pearson's correlation test. p values <0.05 (two tailed) were considered significant.

RESULTS

Serum leptin; adiponectin levels and leptin/adiponectin ratio were significantly higher in the RA group as compared to age matched control group (Table 1) in addition CRP, anti-CCP and RF were higher significant in patients group. Also a significant deference there was in lipid profile and AIP.

Negative significant correlation founded between leptin/adiponectin ratio and CRP; RF; anti- ccp also between AIP and RF; anti-ccp. On the other hands a positive significant correlation was found between AIP and leptin/adiponectin ratio; leptin; adiponectin and CRP (Table 2).

DISCUSSION

In general the chronic of inflammatory associated with an increase of cardiovascular disease development and in RA there's a pro-inflammatory environment that contributes to increase severe disorders of cardiovascular (Goodson *et al*, 2005). In previous studies by other researchers were reported that leptin/adiponectin ratio to a greater extent than leptin and adiponectin alone (Teta *et al*, 2008).

This study showed a significant increase in Leptin and Adiponectin levels in the serum of RA patients compared to healthy subjects. This was in accordance with other studies, who found significantly higher serum Leptin and Adiponectin level in RA patients compared to healthy group (Patrick and Ahmed, 2013). Also, another study detected marked increase in the production of leptin

Table 1 : The characteristics of RA patients and control groups.

Biochemical parameters	RA Group (n=65)	Control Group (n=40)	P- value
Age (year)	45 \pm 0.33	44 \pm 0.57	>0.01
Leptin (ng/mL or ig/L)	29.68 \pm 9.93	12.66 \pm 3.15	<0.001
Adiponectin (ig/L)	21.43 \pm 11.17	9.81 \pm 4.08	<0.001
Leptin/Adiponectin ratio	1.84 \pm 1.09	1.54 \pm 0.90	<0.01
CRP (mg/L)	20.18 \pm 8.25	4.24 \pm 0.60	<0.001
Anti-ccp (U/mL)	104.35 \pm 14.56	17.54 \pm 4.29	<0.001
RF (IU/mL)	84.77 \pm 27.22	8.07 \pm 2.39	<0.001
Total cholesterol (mg/dL)	203.02 \pm 51.43	175.42 \pm 40.67	<0.001
Triglyceride (mg/dL)	165.51 \pm 48.88	143.19 \pm 30.14	<0.001
HDL-cholesterol (mg/dL)	42.98 \pm 11.20	50.77 \pm 16.68	>0.01
AIP	0.45 \pm 0.35	0.37 \pm 0.07	<0.001

P-values <0.05 was considered statistically significant*

Table 2 : Correlation of leptin/adiponectin and biochemical parameters of RA patients

	r	P-value
Leptin/ Adiponectin & CRP	-0.519	<0.0001
Leptin/ Adiponectin & RF	-0.234	<0.0001
Leptin/ Adiponectin & anti-ccp	-0.272	<0.0001
AIP & Leptin/ Adiponectin	0.4503	<0.0001
AIP & Leptin	0.291	<0.0001
AIP & Adiponectin	0.215	<0.0001
AIP & RF	-0.723	<0.0001
AIP & CRP	0.438	<0.0001
AIP & anti-CCP	-0.617	<0.0001

and adiponectin in synovial tissue and synovial fluid in RA patients hence; it is supposed that leptin and adiponectin was produced not only by macrophages, but also by synovial fibroblasts and other inflammatory cells (Patrick and Ahmed, 2013). Elevated leptin levels in RA patients are related with stroke and myocardial infarction that considers factors of cardiovascular risk (Vadacca *et al*, 2011) also, elevated adiponectin level in RA patients may be inhibits anti-atherogenic role of adiponectin.

The observation of present study exist a dyslipidemia and a higher atherogenic index (AIP) in women with RA and that computable with results reported by of other researchers (Asitava and Abhishek, 2016; Silpa *et al*, 2018). RA patients have high levels of inflammation that leads to oxidative changes alter HDL structure and also, presence of hypertriglyceridemia will increase activity of lipase enzyme, which increase degradation or catabolism of HDL that correlate to increase risk of CVD (Schicheng and Rongsheng, 2017). Additionally, hypertriglyceridemia in RA women can explain by cytokines effects at adipose tissue, which increase free fatty acid and lipoprotein lipase activity at the vascular endothelium will reduce. On the other hands, AIP reflect the actual relationship between triglyceride and HDL concentration which predetermine protective and atherogenic lipoprotein. So that AIP consider a predictable marker of CVD (Jayavaishnavi and Padmavijayasree, 2019).

CONCLUSION

There is a positive correlation between AIP and leptin; adiponectin and leptin/ adiponectin ratio with highly significant these observation suggest the patients with RA are possible under risk to cardiovascular disease. Therefore leptin/ adiponectin ratio considered as a marker for CVD in RA patients these finding need further investigation to suggest that patients with early RA exhibit raise leptin/ adiponectin ratio may be prone to cardiovascular disease.

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