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RELATIONSHIP BETWEEN PLAQUE PSORIASIS AND ATHEROSCLEROSIS IN IRAQI PATIENTS

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ABSTRACT

Background: To evaluate the state of some biochemical markers and lipid profilein sera of plaque psoriatic patients.
Aim: The aim of this study is to investigate the levels of inflammatory markers and lipid profile in plaque psoriatic and control groups, and their relationship with the plaque psoriasis.
Patients and Methods: The study was conducted on sixty patients with plaque psoriasis and thirty apparently healthy individuals were taken as control group.The sera obtained from the blood were used to determine the level of Leptin, TNF-alpha, IL-6 and hs-CRP concentrations in both groups by enzyme linked immunosorbant assay (ELISA) method. Determination of total serum cholesterol, LDL, VLDL, TG and HDL by enzymatically method. Also determine the correlation of the inflammatory markers with the plaque psoriasis.
Results and Discussion: The results of the present study showed a significant increase($P< 0.001$) in leptin, TNF-alpha, IL-6,hs-CRP concentration and a significant decrease ($P< 0.05$) in HDL in sera of plaque psoriasis group compared with those of the control group.The results of linear regression analysis show a significant positive correlation of leptin, with TNF-alpha ($r = 0.95$, $p< 0.001$), and IL-6 ($r = 0.98$, $p < 0.001$) and CRP with TNF-alpha ($r = 0.92$, $p< 0.001$), and IL-6 ($r = 0.96$, $p < 0.01$) in plaque Psoriasis.
Conclusion: There is relationship between plaque psoriasis and atherosclerosis and a good significant correlation between leptin and lL-6.

INTRODUCTION

Psoriasis is a common, chronic, relapsing disorder reported in 2% of worldwide populations (Kurd *et al*., 2007). The pathogenesisof psoriasis involves abnormal epidermal differentiation, hyper proliferation, and angiogenesis Lowes *et al*., 2007). T-cell–mediated immune response was one of the accepted theories in pathogenesis ofpsoriasis (Boniface *et al*., 2008).Psoriasis shares striking similarities with other systemic inflammatorydiseases, such as rheumatoid arthritis and atherosclerosis. Intriguingly, the typical histological features of the psoriatic plaque with dermal inflammation and leucocyte infiltration aresimilar to those of the atherosclerotic plaque (Armstrong *et al*., 2011). In atherosclerosis, psoriasis, and rheumatoid arthritis, the activation of theinnate immune system starts an inflammatory cascade, particularly involving T helper 1, T helper 17, regulatory T cells, and downstreamexpression of cytokines (Libby *et al*., 2011). Atherosclerotic lesions (atheromata) are asymmetric focal thickenings of the innermost layer of the artery, the intima. They consist of cells, connective-tissue elements,lipids, and debris.Blood-borne inflammatory and immune cells constitute an importantpart of an atheroma, the remainder being vascular endothelial and smooth-musclecells. The atheroma is preceded by a fatty streak, an accumulation of lipid-laden cells beneath the endothelium (Stary *et al*., 1995).Most of these cells in the fatty streak are macrophages, togetherwith some T cells. Fatty streaks are prevalent in young people, never cause symptoms, and may progress to atheromata or eventually disappear. In the center of an atheroma, foam cells and extracellular lipid droplets form a coreregion, which is surrounded by a cap of smooth-muscle cells and a collagen-rich matrix.T cells, macrophages, and mast cells infiltrate the lesion and are particularly abundant in the shoulder region where the atheroma grows (Stary *et al*., 1994; Jonasson *et al*., 1986; Kovanen *et al*., 1995). Many of the immune cells exhibitsigns of activation and produce inflammatory cytokines (Frostegård *et al*., 1999).

The aim of the study: The aim of this study is to investigate the levels of inflammatory markers (Leptin, hs-CRP, TNF-

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alpha, IL-6 and lipid profile in plaque psoriatic and control groups, and determine the relationship between the level of LLeptin, hs-CRP, T NF-alpha, and lL-6 in plaque psoriasis.

MATERIALS

Subjects

The study was conducted over a period of eleven months from October 2012 till August 2013. Samples were collected from the clinic of dermatology in Al-Sadder Teaching Hospital in Najaf City. The laboratory work was performed at the department of biochemistry in College of Medicine /University of kufa. This study included sixty plaque psoriatic patients and thirty healthy individuals taken as a control group. The diagnosis was mainly clinical and done by specialist dermatologist. A questionnaire was designed to obtain the information from psoriasis patients and control group. It included the name, age, weight, height, gender, duration of disease, drugs allergy and smoking. Exclusion criteria were those suffering from other disease (e.g. hypertension, diabetes mellitus, asthma etc.), those who take medication (e.g. methotrexate, diuretics, steroid, etc.) for at least one month before the history, alcoholics, smokers and pregnant women. The psoriasis group comprised sixty adults (32 men and 28 women) andtheir agedmean ± SD of 35.16 ±11.89year.The control group includes thirty apparently healthy individuals (18 men and 12 women) and their aged mean ± SD of 34.56 ± 10.8 year.

Blood Sampling

Venous blood samples were drawn from psoriasis and control subjects by using disposable syringes (5mL) in the sitting position. Five ml of blood were obtained from each subject by vein puncture and pushed slowly into plain disposable tubes. Blood was allowed to clot at 37˚C for 10-15 minutes and then centrifuged at 2000 xg for approximately 10-15 minutes, then the sera were obtained and stored at -20˚C until analysis.

METHODS

Markers of inflammation levels (lipten, hs-CRP, IL-6, TNF-alpha) were estimated by Enzyme Linked Immunosorbant Assay (ELISA) method. Determination of total serum cholesterol, LDL, VLDL, TG and HDL byenzymatic ally method.

RESULTS

The results of the present study showed a significant increase(P< 0.001) in Leptin, TNF-alpha, IL-6 and hs-CRP concentration of psoriasis group compared with those of the control group.The present study showed a significant increase<0.01 in total cholesterol, triglycerides, (P<0.05) VLDL-cholesterol, LDL-cholesterol, and a significant decrease (p<0.05) in HDL-cholesterol concentration in sera of psoriasis group compared to control group as show inTable (1).A positive significant correlation was found between serum Leptin and hs- CRP levels with TNF-alpha and IL-6. in plaque psoriatic patients as show in Table (2). Figure (1) show a good positive correlation representation of serum Leptin with lL-6 (r=0.98 P< 0.001) in plaque psoriatic patients.

Table 1. Mean and standard deviation of Leptin, TNF-alpha, IL-6, hs-CRP and lipid profile concentration in plaque psoriasis and control groups

Subject	No	Parameter	Mean ±SD	P value
Patients	60	Leptin	22.02±10.87	<0.001
Control	30	ng/ml	5.8± 1.76	
Patients	60	Total cholesterol	6.37 ± 0.87	<0.01
Control	30	mmol/L	5.59 ± 0.74	
Patients	60	TNF-alpha	49.63± 27.04	<0.001
Control	30	pg/ml	9.43± 4.04	
Patients	60	IL-6	234.15±79.92	<0.001
Control	30	pg/ml	84.01± 36.03	
Patients	60	hs-CRP	9.52±4.04	<0.001
Control	30	µg/ml	2.05± 0.87	
Patients	60	HDL-cholesterol	1.12± 0.27	<0.05
Control	30	mmol/L	1.49±0.43	
Patients	60	Triglycerides	1.59±0.85	<0.01
Control	30	mmol/L	1.04±0.52	
Patients	60	VLDL-cholesterol	0.77±0.41	<0.05
Control	30	mmol/L	0.48±0.24	
Patients	60	LDL-cholesterol	4.34±0.93	<0.05
Control	30	mmol/L	3.72±0.92	

P< 0.05 was considered to be statistically Significant

Table 2. linear regression analysis of Leptin, and CRP with TNF-α, and IL-6 in plaque psoriasis

Parameter	IL-6		TNF-alpha	
	r	P	r	P
Leptin	0.98	0.001	0.95	0.001
CRP	0.96	0.001	0.92	0.001

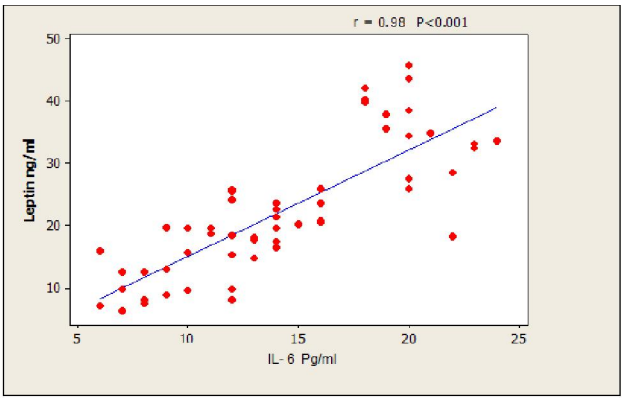

Figure 1. The correlation of Leptin concentration with IL-6 score in plaque psoriasis

DISCUSSION

Leptin has an vital role in inflammationand in immune regulation. It activates monocyte/macrophage cells and potentiates production of the proinflammatory cytokines, tumor necrosis factor-alpha (TNF-alpha), IL- 6, and direct T cell differentiation to Th1 phenotype (Moon *et al*., 2013). The results of the present study were in agreement with Amira *et al*. (2010), who found that a group with psoriasis have higher levels of the obesity-associated hormone (Leptin) than those without psoriasis. They also disagree with Aktan *et al*. (2007), who found that there was no significant difference between serum Leptin levels of psoriatic patients and control group. TNF-alpha(1) modulates cell growth, differentiation(2) leads to cachexia by inhibiting stimulation of liver lipogenesis and stimulating lipolysis (3) initiates apoptosis of degenerated cells, neoplastic cells or virus-infected cells, and (4) produces inflammation (Tracey *et al*., 1989). Monocytes and macrophages are the main cellsrelated to the production of TNF-α, but other immunecells are also capable of synthesizing

it such as, basophils, eosinophil's, neutrophils and T and B lymphocytes (Vassalli, 1992). Tumor necrosis factor is a pleiotropiccytokine that has multiple proinflammatory and co stimulatory effects on a broad range of cell types (Turner *et al*., 1989). Activated T cells, monocytes, and pro-inflammatory cytokines, most notably TNF-alpha, have all been shown play pivotal roles in the pathogenesis of psoriasis (Boyman *et al*., 2007). IL-6 is a pleiotropic cytokine. Its typical actions are the regulation of theexpression of other cytokines, cell proliferation anddifferentiation and inhibition of tumor growth, as wellas stimulation of acute-phase proteins in the inflammatory reaction. IL-6 is present in normal human skin andis immunologically detected in basal keratinocytes, endothelial cells, fibroblasts and mononuclear cells (Castells-Rodellas *et al*., 1992). The difference between IL-6 levels in cases and controls was significant (P<0.001). This was in agreement with other studies by Abanmi *et al*. (2005) who found increased levels of IL-6 in their patients but different results were reported by Jacob *et al*. (2003) who found no difference in serum IL-6 levels.IL-6 mediates T-cell activation, stimulates proliferation of keratinocytes and, at the start of acute inflammation, mediates the acute phase responses Paquet *et al*. (1996). Goodman *et al*. observed increased IL-6 levels in psoriatic lesions, compared to the common skin of healthy group (Goodman *et al*., 2009).

C-Reactive Protein (CRP), a positiveacute phase protein, is released in response to increasedlevels of cytokines, such as IL-6 and TNF-α, and patients with elevated levels of CRP seem to exhibitan increased risk for adverse cardiovascular outcome (Koenig *et al*., 2006).The results of the present study were in agreement with other studies, (Amina, 2009; Gurkok *et al*., 1999; Reynoso-von Drateln *et al*., 2003) they showed that lipid profile in psoriatic patients undergoes some considerable changes in which the levels of total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglycerides were significantly increased and decreased HDL-cholesterol concentration. The activation of the immune system in psoriasis may cause some changes in lipid profile of patients. However, these changes may be related to some abnormalities of the digestive system. The digestive system takes part in the decomposition, modification, and synthesis of many organic compounds, including lipids. In psoriatic patients, structural and functional abnormalities have been found in nearly all the segments of the gastrointestinal tract (Pietrzak *et al*., 1998). The correlation between serum leptin and lL-6 found for the patients with psoriatic can be considered as a parameters which may be beneficial in those patients and could be used to predict the progression ofplaque psoriatic patients.

Conclusion

There is an association between the inflammatory markers and psoriasis. AlsoThese are important risk factors in the development of coronary artery diseasein psoriatic patients.Complete lipid profile is always advisable for psoriatic patients.There was a good positive correlation between serum leptin and lL-6 level in patients with plaque psoriatic

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