Levels of Interleukine-8 and Some Antioxidants in Serum of Patients with Osteoarthritis.

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ABSTRACT:

BACKGROUND:

Osteoarthritis is a form of arthritis that features the breakdown and eventual loss of the cartilage of one or more joints. Cartilage is a protein substance that serves as a "cushion" between the bones of the joints. Among the over 100 different types of arthritis conditions, osteoarthritis is the most common, affecting over 25 million people in the United States. Osteoarthritis occurs more frequently as we age. Osteoarthritis is abbreviated as OA or referred to as degenerative arthritis or degenerative joint disease (DJD). Osteoarthritis commonly affects the hands, feet, spine, and large weight-bearing joints, such as the hips and knees. Osteoarthritis usually has no known cause and is referred to as primary osteoarthritis. When the cause of the osteoarthritis is known, the condition is referred to as secondary osteoarthritis.

OBJECTIVE:

The main objective of this study is to evaluate the association between the levels of Interleukin-8 and some antioxidant in patients with OA.

PATIENTS AND METHODS:

This study was performed during the period from April 2010 to February 2011, and included 50 patients with OA according to the American College of Rheumatology ACR 1990; their age range from 40-60 years with mean age of 46.66 ± 2.83 years. These patients were matched by age and sex to 25 healthy control subjects with the mean age of 48.32 ± 2.92 years. Blood samples were taken from each individual and separated for the estimation of IL-8 and some antioxidants levels using enzyme – liked immunosorbent assay (ElIZA) technique and colorimetric method. The laboratory tests were done in Teaching Laboratories of the Medical City and the Department of Physiological Chemistry / College of Medicine University of Baghdad.

RESULTS:

The level of IL-8 and Ceruloplasmin (CP) in serum of patients with OA was significantly higher than in serum of healthy control while the level of Glutathione (GSH) and S.uric acid in serum of OA patients was significantly higher than healthy control and there is no significant difference in level of serum albumin between the patients and control.

CONCLUSION:

It is clear from this study that there is a relationship between the levels of IL-8, CP, GSH, and S.uric acid concentrations and OA while there is no relationship between S.albumin concentration and OA disease.

KEY WORD: IL-8, CP, GSH, S.uric acid, S.albumin and osteoarthritis disease.

INTRODUCTION:

Osteoarthritis (OA) also known as degenerative arthritis or degenerative joint disease is a group of mechanical abnormalities involving degradation of joints, including articular cartilage and subchondral bone. Symptoms may include joint pain, tenderness, stiffness, locking, and sometimes an effusion. A variety of causes hereditary, developmental, metabolic, and mechanical may initiate processes leading to loss of cartilage. When bone surfaces become less well protected by cartilage, bone may be exposed and damaged. As a result of decreased movement secondary to pain, regional muscles may atrophy, and ligaments may become more lax. The main symptom is pain, causing loss of ability and often stiffness. "Pain" is generally described as a sharp ache, or a burning sensation in the associate muscles and tendons. OA can cause a crackling noise (called "crepitus") when the affected joint is moved or touched, and

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patients may experience muscle spasm and contractions in the tendons. Occasionally, the joints may also be filled with fluid. Humid and cold weather increases the pain in many patients. (1)

OA commonly affects the hands, feet, spine, and the large weight bearing joints, such as the hips and knees, although in theory, any joint in the body can be affected. There are two type of OA primary, this type of OA is a chronic degenerative disorder related to but not caused by aging, as there are people well into their nineties who have no clinical or functional signs of the disease and secondary, This type of OA is caused by other factors but the resulting pathology is the same as for primary OA: Congenital disorders of joints, Diabetes, Inflammatory diseases, Injury to joints, Septic arthritis, Obesity, Ligamentous, Marfan syndrome, Alkaptonuria, Hemochromatosis and Wilson's disease[2].

Interleukin-8 belongs to a new family of chemotatic peptide called chemokines, this proinflammatory mediator is secreted by different cells such as monocytes, neutrophiles, endothelial cells, fibroblast after activation, and by mitogen-stimulated T-lemphocytes. IL-8 is a key cytokine that has been found in scales of osteoarthritis, in fluid of patients suffering from rheumatoid arthritis and gout [3].

Cytokines are considered to play a role in the pathogenesis and clinical manifestations of OA. Some of the cytokines like tumor necrosis factor-alpha (TNF-a), IL-1, IL-6, and IL-8 are considered to be involved in the regulation of the sympathetic nervous system and to be associated with the symptoms of fatigue, pain sleep, and stress responses [4].

Ceruloplasmin (CP) is a metalloprotein with six to eight copper atoms. Ceruloplasmin resembles albumin are regarded primarily as transport proteins CP transport Cu in the plasma and have a multiple biochemical activities including, scavenging of superoxide anion radical's (Ó2). CP is one of the acute phase protein and the majority of the antioxidant CP activity in serum is depend on the level of Cu containing proteins [5].

Glutathione is the important of nonprotein cellular thiol compound occurs in many different cells of humans. Glutathione is a tripeptide consisting of three amino acids (glycine, cystein, glutamic acid). Function of glutathione is to regulate (oxidation – reduction) reactions because it's protection for some antioxidant compound like ascorbic acid. Glutathion functions include the detoxification of xenobiotics, carcinogens, free radicals, and peroxides; regulation of immune function; and maintenance of protein structure, function and turnover[6].

Uric acid have an antioxidant ability both by binding iron and copper ions in form that do not accelerate free radical reactions by directly scavenging oxidizing species such as (Ó2) and peroxyl radical. Reaction of uric acid with oxidizing species, can generate uric acid radical that are capable of causing biological damage [7].

Albumin is the major protein of human plasma (3.3-4.7 g/dl) and make approximately 60% of total plasma proteins. Liver synthesized about 12 g of albumin per day, and its synthesized as a preproprotein. The synthesis of albumin is depressed in a variety of disease particularly those of the liver [8].

PATIENTS AND METHODS:

The prospective study comprised 50 Iraqi patients fulfilling the ACR criteria for the diagnosis of OA, their mean age 46.66± 2.83 years.

Another 25 healthy individuals who are age and sex matched with the patients.

Blood samples were taken from individuals in both groups for estimating IL-8, CP, GSH, uric acid, and albumin levels.

Laboratory investigation which include: Hemoglobin (Hb), Erythrocyte sedimentation rate (ESR) was done in Laboratory Teaching center of Baghdad Hospital.

The study was based on the immunological assay of IL-8 with ELIZA, and it's a two step sandwich type assay, and Cp, GSH, uric acid, and albumin levels were estimated with colorimetric method.

Statistical analysis:

Descriptive statistics for all data of each set were expressed as a mean ± SD. And compared using independent sample (t) test $p<0.05$ were considered statistically significant. The overall productive values for the results in studied groups were performed according to program of office xp.

RESULTS:

The characteristics of 50 patients of OA and 25 controls are shown in table (1).

Table 1: Characteristics of OA patients and controls

Parameters	Patients (N = 50) Mean ± SEM	Control (N= 25) Mean ± SEM	P-value	Sig.
Age (y)	46.66± 2.83	48.32 ± 2.92	0.45	NS
BMI (kg/m2)	29.62 ± 0.81	28.31 ± 0.79	0.30	NS

Values are the (mean±SD), BMI=body mass index, OA= Osteoarthritis, NS=not significant, and N=number of samples.

The mean values of IL-8 and CP levels in serum of patients with OA were significantly higher as compared to the level in serum of healthy control group ($P < 0.01$), and the mean values of GSH and uric acid levels were significantly lower ($p<0.05$) in serum of patients with OA than in healthy control, while there was no significant difference ($p>0.05$) in levels of serum albumin between OA and healthy control As shown in table (2).

Table 2: Serum IL-8, CP, GSH, uric acid, and albumin levels (mean ± SD) in patients with OA (N=50) and controls (N=25).

Parameters	Patients (N=50) Mean ± SEM	Control (N=25) Mean ± SEM	(P-value)	Sig.
IL-8 (pg/ml)	139.62 ± 0.203	75.33 ± 0.274	0.001	HS
CP (mg/dl)	26.21 ± 0.81	21.87 ± 0.572	0.001	HS
GSH (µmol/l)	0.361± 0.04	0.601 ± 0.09	0.05	S
S.uric acid (mg/dl)	4.251 ± 0.302	4.951 ± 0.879	0.05	S
S. albumin (g/dl)	3.501 ± 0.221	3.621 ± 0.584	0.08	NS

DISCUSSION:

In this study there was a significant increase of IL-8 level in the serum of OA patients and the study was in agreement with previous studies [9], which found that Interleukin 8 (IL-8) is a member of the alpha chemokine family of cytokines originally identified as a neutrophil chemoattractant. Recently, they reported that elevated levels of IL-8, correlated with increased bone metastasis and hypothesized that IL-8 also directly stimulated the differentiation of human peripheral blood mononuclear cells into bone-resorbing osteoclasts, also IL-8 was able to stimulate human osteoclast formation and these results demonstrate a direct effect of IL-8 on osteoclast differentiation and activity [(9)].

This study also showed a significant increase of CP levels in serum of patients with OA, Ceruloplasmin used as a measure of acute phase reactivity, during inflammatory states, it acts as an antioxidant through scavenges the free radical species and thus protects surrounding cells against oxidative damage [(10)].

Osteoarthritis is an inflammatory disorder of the joint. Lipid peroxidation mediated by free radicals is considered to be the major mechanism of cell membrane destruction and cell damage. Free radicals are formed in both physiological and pathological conditions in mammalian tissues [(11)]. The uncontrolled production of free radicals is considered as an important factor in the tissue damage induced by several pathophysiologies [(12,13)]. Antioxidants are compounds that dispose, scavenge, and suppress the formation of free radicals, or oppose their actions [(14)]. Since, even modern therapy has provided only limited success in preventing joint destruction, the role of antioxidants as adjunctive therapy seems warranted as they plays an effective role in protecting the biological tissues below a critical threshold of reactive oxygen species [(15)] and constitute a mutually supportive team of defense against reactive oxygen species (ROS).

GSH levels was significantly decreased in the serum of OA patients and this study was in agreement with a study done by Y. Wang, et.al [(16)], showed that joint fluid from patients with osteoarthritis was characterized by significantly decreased superoxide dismutase levels and significant decreases in glutathione compared to the reference group.

And also in agreement with another study of Surapaneni KM, et.al [17], showed that glutathione, superoxide dismutase and Catalase are the key antioxidants that defend our bodies against free radicals. A deficiency can be responsible for many of the degenerative disease states including osteoarthritis. Several studies have shown the key role that these antioxidants play in osteoarthritis[18].

Uric acid and albumin account for the major contributions of total antioxidant capacity in human serum. Uric acid deficiency can agree with a study [19], showed that uric acid can be oxidized following the nonenzymetic degradation, and has been proven to be selective antioxidant, capable especially, of reacting with hydroxyl radicals [18]. And there was no significant difference of albumin level in serum of patients with OA, that serum albumin was shown to be decreased with the increased disability and score, and it is might be due to the more consumption and utilizing of the free radical species and it's oxidizing environmental effects [20].

CONCLUSION:

It is clear from this study that there is a relationship between the levels of IL-8, CP, GSH, and S.uric acid concentrations and OA while there is no relationship between S.albumin concentration and OA disease.

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