



# Study the Level of Cartilage Acidic protein (CRTAC1) in Serum of Iraqi Patients with osteoarthritis

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## Abstract

Osteoarthritis, often known as OA, is defined by the deterioration of articular cartilage, limited intraarticular inflammation with synovitis, and alterations in the peri-articular and subchondral bone. This study measured CRTAC1, CRP, ESR, Vitamin D3, Mg, Calcium, and Lipid profiles in Osteoarthritis patients. The current study comprised a total of 130 participants, who were divided into two groups. Group1 contained 90 Osteoarthritis patients, and group2 controls 40; the samples were extracted from female and man, the levels, CRTAC1, CRP, ESR, Vitamin D3, Mg, Calcium, Cholesterol, TG, VLDL, LDL, and HDL were evaluated. The levels of CRTAC1, CRP and, Vitamin D3 were determined using an enzyme-linked immunosorbent assay (ELISA), and the stories, Mg, Calcium, Cholesterol, TG, VLDL, LDL, and HDL were assayed using a Human Reader HS Device. Westergren method was used to analyze the level of ESR. The result of CRTAC1 shows a high significant change among two groups OA patients and control. Serum vitamin D3 and CRP value have high significant change in their levels in osteoarthritis patients. Serum levels of Triglyceride, HDL, Mg, Ca, ESR and VLDL showed a significant changes between two groups OA patient and control. Cholesterol and LDL values have non-significant variation in their levels in osteoarthritis patient's comparison with control.

## Conclusion

According to the presented results CRTAC1, CRP, ESR, Vitamin D3, Mg, Calcium, T.G, VLDL, and HDL do affect by Osteoarthritis patients. LDL and cholesterol do effect osteoarthritis patients.

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## Introduction

Osteoarthritis, often known as OA, is a degenerative and incapacitating musculoskeletal condition that affects millions of individuals throughout the world and contributes significantly to the expense of providing medical care. Deterioration of the articular cartilage, production of osteophytes, subchondral sclerosis, synovial inflammation, and ultimately loss of joint function are the hallmarks of this type of arthritis, which is the most frequent form of the disease (1). Occurring most commonly in the hands, hips,

and knees, osteoarthritis is a collection of disorders that are distinguished by the breakdown of articular cartilage and the presence of ongoing pain (2). When a person has (OA), the cartilage that is found within a joint will start to deteriorate, and the bone that is found underneath will start to slowly change, which will get worse over time (3). The clinical evidence also reveals that osteoarthritis frequently co-exists with metabolic illnesses and comorbidities such as diabetes mellitus and cardiovascular diseases, both of which are predictive of rapid deterioration of the OA joint.

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In a recent systematic review, osteoarthritis risk factors were used to identify six clinical phenotypes. These phenotypes include chronic pain (with a prominent central mechanism), inflammation, metabolic syndrome, bone and cartilage metabolism, mechanical overload, and minimal joint disease (4). Osteoarthritis is the most common form of arthritic joint disease and a leading cause of disability and joint pain around the world. OA is a multifactorial disease that is affected by aging, joint trauma, bio-tribology of joint contact surface, genetic susceptibility, obesity, and metabolic deregulation (5). The most prominent clinical signs of OA are a deterioration of the articular cartilage as well as alterations in the structure of the subchondral bone. When cartilage in a joint is completely lost as a result of a disruption in cartilage homeostasis caused by the induction of catabolic factors as well as the down-regulation of anabolic factors, the bones and soft tissue structures that surround the joint are altered. This can lead to joint pain, swelling, deformity, and disability (6). Articular cartilage, subchondral bone, and the synovial membrane that lines the afflicted joint are the primary tissue types that are impacted by osteoarthritis. The disease can affect any and all tissues found within a joint. The advancement of osteoarthritis is ultimately caused by changes in the physiological processes that are taking place in these tissues. Osteoblasts and osteoclasts are the two primary types of cells that can be found in the subchondral bone, and both are of great relevance in the study of OA. Alterations in the usual cellular processes lead

to abnormal bone remodeling, which can result in sclerosis and the development of osteophytes (7). An example of a problem that affects the musculoskeletal system is osteoarthritis, which causes irreparable damage to joint function as a result of aging, trauma, wear and tear on cartilage, and chronic inflammation in the joints. X-ray radiography makes it possible to make an accurate diagnosis of osteoarthritis, which is defined by the progressive narrowing of joint space, the development of osteophytes, the sclerosis of the subchondral bone, and the creation of cysts (8). In osteoarthritis, dysregulation brought on by the presence of a variety of biofactors leads to the loss of cartilage homeostasis, which in turn results in the degradation of the collagen- and proteoglycan-rich extracellular matrix (ECM), fibrillation and erosion of the articular surface, cell death, matrix calcification, and vascular invasion (9).

## **Materials and Methods**

### **Patients' selection**

The study was carried out at the Kindy Hospital/Baghdad for the period from November 2021- January 2022. We studied 90 OA patients and 40 controls. a total of 5 milliliters of venous blood was drawn from the patient, and the parameters under study were then evaluated. An enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of CRTAC1, CRP, and Vitamin D3. A Human Reader HS Device was used to analyze the levels of Mg, Calcium, Cholesterol,



TG, VLDL, LDL, and HDL. Westergren method

was used to analyze the level of ESR .

### Inclusion Conditions

All patients with Osteoarthritis were diagnosed clinically and by X-ray.

### Exclusion Criteria

Patients with other inflammatory disease, Diabetic patients and patients with Thyroid diseases were excluded from the study.

### Statistical analyses

The statistical analysis tool was used to perform the analysis on the data (SPSS 25). The T-test was used to the data that had a normal parametric distribution and alpha levels of 0.05.

### Result and Discussion

Table (1) showed the mean  $\pm$ SE of BMI and WC in patients and control [(30.31Kg/m<sup>2</sup> $\pm$  0.64) (24.93 kg/m<sup>2</sup>  $\pm$  0.42)] [(100.71cm $\pm$ 1.28) (84.05cm  $\pm$  1.43)] respectively, there is a high significant alteration in BMI and WC among patients OA and controls, where the result indicates a high significant difference among two groups (P $\leq$ 0.01).

In study by Vasilic - Brasnjevic S, et al. (10), WC was significantly different between patients with OA and controls, and this difference was statistically high.

**Table (1)** Comparison between patients and control groups in BMI and WC.

Group	Mean $\pm$ SE	
	BMI (kg/m <sup>2</sup> )	WC (cm)
Patients	30.31 $\pm$ 0.64	100.71 $\pm$ 1.28
Control	24.93 $\pm$ 0.42	84.05 $\pm$ 1.43
T-test	1.989 **	4.256 **
P-value	0.0001	0.0001

\*\* (P $\leq$ 0.01).

The BMI in patients was significantly (P=0.0001) high in patients than control group (30.3Kg/m<sup>2</sup>-24.9Kg /m<sup>2</sup>) respectively.

The result of CRTAC1 showed a high significant variance (P $\leq$ 0.01). The mean  $\pm$ SE for patients OA and control were [(119.26 ng/ml  $\pm$ 3.14) (47.84 ng/ml  $\pm$ 1.23)] respectively. As shown in Table (2).

A study that was carried out in 2021 discovered that (CRTAC1) was the factor that was most strongly associated with both the diagnosis of osteoarthritis (odds ratio 1.46 [95 percent confidence interval 1.41 -1.52] for knee OA, odds ratio 1.36 [95 percent confidence 1.29-1.43] for hip OA, and odds ratio 1.33[95 percent confidence interval 1,26 -1.40] for hand OA, and progression to joint replacement, based CRTAC1 was not shown to be related with any of the other inflammatory arthritis types. Patients who had joint replacement surgery before their plasma samples were taken were found to have a certain protein profile (11).

The result of CRP presented a high significant change (P $\leq$ 0.01).The mean  $\pm$ SE for patients OA and control were [(13.42 ng/dl  $\pm$ 0.31) (4.94 ng/dl  $\pm$ 0.23)] respectively. As shown in Table (2).



In the study by Tootsi K, et al (12) also discovered that the OA group had a greater high sensitive C-reactive protein (hs-CRP) level compared to both the patients and the controls.

**Table (2):** Comparison between patients and control groups in CRTAC1 and CRP.

Group	Mean ± SE	
	CRTAC1 (ng/ml)	CRP (ng/ml)
Patients	119.26 ±3.14	13.42 ±0.31
Control	47.84 ±1.23	4.94 ±0.23
T-test	11.493 **	0.964 **
P-value	0.0001	0.0001
** (P≤0.01)		

The results of Vit D3 showed mean ±SE of OA patients and control [(35.20ng/ml ±1.26) (65.11ng/ml ±2.22)] respectively, there was shows a high significant variation between two groups in Vitamin D3 (P≤0.01) as shown in Table (3). The effect of one's vitamin D status on the onset or progression of (OA). It is believed that a lack of vitamin D might impact the chondrocytes, which in turn can damage the quality of the articular cartilage, leading to an increase in PTH as well as bone turnover. Because vitamin D causes the mature articular cartilage to produce more proteoglycan, it has the potential to influence the metabolic processes of the mature articular cartilage (13). The results of Calcium (Ca) were presented in Table (3).which revealed a significant variance (P≤0.01), between OA patients and control [(8.24 mg/dl ±0.18) (9.12mg/dl ±0.11)] respectively.

In the research carried out by Payment M and colleagues (14), the researchers discovered that the serum calcium content has an inverse connection with radiographic OA of the knee. The presence of a high calcium level may

possibly play a protective effect in the management of radiographic knee osteoarthritis.

The results of Magnesium (Mg) showed a significant variance (P≤0.05).The mean ±SE for patients and control were [(0.567mg/dl ±0.02) (0.637mg/dl ±0.02)] respectively. As shown in Table (3).

Wu Z, et al. in their study (15). A higher magnesium intake was not associated with a lower incidence of knee osteoarthritis erosive in this study. However, in patients with knee osteoarthritis erosive, there may be an inverse relationship between an increased daily magnesium intake and the risk of fracture.

**Table (3)** Comparison between patients and control groups in Ca, Mg and D3.

Group	Mean ± SE		
	Ca (mg/dl)	Mg (mg/dl)	D3 (ng/ml)
Patients	8.24 ±0.18	0.567 ±0.02	35.20 ±1.26
Control	9.12 ±0.11	0.637 ±0.02	65.11 ±2.22
T-test	0.556 **	0.059 *	4.758 **
P-value	0.0022	0.0204	0.0001

Regarding ESR the results revealed a high significant variation among two groups (P≤0.01) (30.41mmol/hr ± 1.93) (19.97 mmol/hr ± 2.16) as shown in Table (4).

Hanada M, et al in their study (16), The ESR levels of individuals who had KOA were greater than the ESR levels of patients who did not have knee osteoarthritis .



**Table (4)** Comparison between patients and control groups in ESR.

Group	No	Mean ± SE of ESR (mmol/hr)
Patients	90	30.41 ± 1.93
Control	40	19.97 ± 2.16
T-test	--	6.394 **
P-value	--	0.0016

\*\* (P≤0.01).

The results of Lipid profile were presented in Table(5).The result of TG revealed a significant change (P≤0.01), mean ± SE among patients OA patients and control [(123.74 mg/dl ±3.28)(107.68 mg/dl ±2.85)] respectively.

The result of Cholesterol presented a non-significant alteration (P>0.05). The mean ±SE for OA patients and control were [(155.61mg/dl ±4.15) (152.45mg/dl ±4.85)] respectively

The result of VLDL showed a significant variance (P≤0.01). The mean ±SE for OA patients and control were [(25.19 mg/dl ±0.78) (21.54 mg/dl ±0.57)] respectively.

The HDL results shows a significant variance (p< 0.05) among the OA Patients and healthy control [(48.64mg/dl ±3.09) (39.04mg/dl ±0.87)] respectively.

The result of LDL showed a non-significant change (P>0.05). The mean ±SE for OA patients OA and control were [(87.44mg/dl ±3.13) (91.87mg/dl ±4.63)] respectively.

In a study by Tootsi K, et al (12), there was no discernible difference in total cholesterol or low-density lipoprotein (LDL) cholesterol levels between the groups that participated in the trial. In comparison to the control group, the OA group had significantly lower levels of high-density lipoprotein (HDL) cholesterol and greater levels of triglycerides in their blood.

**Table (5)** Comparison between difference groups in Lipid profile.

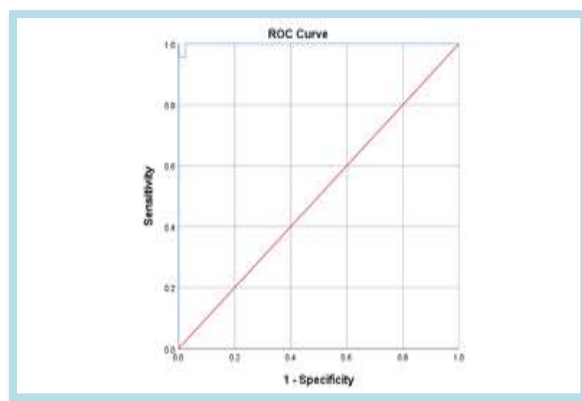
Group	Mean ± SE (mg/dl)				
	Triglyceride	Cholesterol	VLDL	HDL	LDL
Patients	123.74 ±3.28	155.61 ±4.15	25.19 ±0.78	48.64 ±3.09	87.44 ±3.13
Control	107.68 ±2.85	152.45 ±4.85	21.54 ±0.57	39.04 ±0.87	91.87 ±4.63
T-test	10.454 **	13.907 NS	2.456 **	9.273 *	11.131 NS
P-value	0.0029	0.654	0.0038	0.0425	0.431

\* (P≤0.05), \*\* (P≤0.01).

### The receiver operating characteristics curve (ROC).

ROC is a statistical analysis that plots the relationship between sensitivity and specificity to discover the best specificity and sensitivity for a diagnostic test. 1. Precision (17).

ROC test for CRTAC1 marker showed very clear cut off value with 100% sensitivity and 97% specificity that indicates CRTAC1 considered as a good diagnostic marker. As shown in chart (1).



**Chart 1:** ROC curve for CRTAC1

### Conclusion

The result of CRTAC1 shows a high significant change among two group's patients OA and control. In our study, the high concentration of CRTAC1 in patients compared to healthy people showed that it can be considered as a marker in the diagnosis of the disease osteoarthritis.



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