Research Article

Evaluation of Serum Interleukin-6, Body Mass Index and bone mineral density in Patients with Nodal Osteoarthritis

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Abstract

Background: Nodal osteoarthritis is a type of osteoarthritis and its common worldwide, the etiology is unknown but there are a biochemical markers recognized. Many studies have explain that adiponectin have an important role in the pathogenesis of osteoarthritis, but little is studied about the relation between serum Interleukin-6 , body mass index and bone minerals density with nodal osteoarthritis.

Objectives: To evaluate serum level of Interleukin-6 , body mass index and bone minerals density in nodal osteoarthritis patients.

Methods: Sixty patients with nodal osteoarthritis and sixty controls were included in the study; serum Interleukin-6, body mass index and bone mineral density were measured in all subjects. Student t-test was applied to find out the significant difference between two means.

Result: This study shows a significant increase in body mass index (BMI) in those patients with nodal osteoarthritis (mean $\pm$ SD) (31.6 $\pm$ 8.7) , P-value < 0.05. the mean of serum IL-6 is significantly increased in patients (mean $\pm$ SD) (3.2 $\pm$ 2.2) P-value < 0.05 . but not in control group and there's an obvious decrease in the bone mineral density between nodal osteoarthritis patients and control group(mean $\pm$ SD)(-2.2$\pm$ -1.1) P-value < 0.05.

Conclusion: This study shows the role of Interleukin-6 as inflammatory mediator in nodal osteoarthritis and osteoporosis. The BMI has a role in Interleukin-6 level and it's increased in nodal osteoarthritis patients.

Key words: body mass index, Nodal osteoarthritis, serum Interleukin-6.

INTRODUCTION

Osteoarthritis (OA) is a heterogeneous group of disease containing a different spectrum of clinical symptoms and signs. In generalised OA the hand is commonly involved, and polyarticular interphalangeal OA is taken as the marker for predisposition to OA at multiple sites(1).

Nodal OA (NOA), a type of OA, which is a degenerative disease of cartilage that covers the bone surfaces at the joints which begins to wear out, it characterized by polyarticular interphalangeal and thumb base of hand with Heberden's and Bouchard's nodes formation ,it is more common in women, and there is a clear genetic predisposition(1).

The incidence of hand osteoarthritis in people over 55 years of age was 13.4% for men and 26.2% for women, and these levels are increased with age(2).

The pathogenesis of OA appears to be the result of interaction between mechanical, cellular, and biochemical forces ,cytokines like tumor necrosis factor-α and interleukin-6, and even fragments of the cartilage itself induce chondrocytes to be differentiated (3).

As a result, these cells increase their synthesis of matrix metalloproteinases (MMPs) that cause the loss of

proteoglycans, at the same time, a decrease in tissue Inhibitors of Matrix Metalloproteinases (TIMPs) occurs (4).

Interleukin-6 (IL-6) is a substance produced by blood cells T-cells, as well as macrophages and endothelial cells (5). However, IL6 is a cytokine, and it is involved in relaying information between cells as both a signaling molecule and a signaling protein. IL-6 may behave as both an anti-inflammatory agent and a pro-inflammatory mediator, depending on certain conditions (6).

IL-6 plays an important role in regulating cell growth as well as immune function. In fact, its release is triggered by tissue damage or infection. Receptor sites are found on the surface of numerous cells throughout the body. From these sites, interleukin-6 transports a variety of proteins through the three major signal transduction pathways: protein kinase C, cAMP/protein kinase A, and calcium release also each IL-6 molecule performs a specific action, depending on the cell that initiated its release (6).

IL-6 is also known as a myokine, a type of cytokine triggered by muscle contraction and then discharged into the blood stream, this exchange promotes a variety of biologic actions. For one thing, it increases the breakdown of fats. It also improves insulin resistance, resulting in better uptake and utilization of glucose. Therefore, IL-6 therapy may have an application in treating certain conditions, such as obesity and diabetes type II (7).

IL-6 is considerd as the best marker for function of Immune system, impaired or uncontrolled IL-6 gene expression can produce unwanted immune responses and lead to a variety of diseases, including autoimmune disorders. Patients with rheumatoid arthritis, for example, typically have elevated levels of IL-6 in their synovial tissue. To combat this dysfunction, researchers continue to investigate different ways to inhibit binding of interleukin-6. This includes development of an anti-IL-6 receptor antibody (8).

This study is aimed to evaluate the serum IL-6, body mass index and bone mineral density in patients with nodal osteoarthritis

PATIENTS AND METHODS

One hundred twenty (60 patients with NOA & 60 healthy controls) were enrolled in this study. The patients studied in this case-control study have been selected from patients attended Rheumatology and Rehabilitation Out-Patient Clinic, In Al-Yarmouk Teaching Hospital during the period from November 2014 to February 2015.

They were randomly selected, diagnosed clinically and radiologically. Many laboratory tests have been done for each patients to exclude other possible causes of arthritis, these tests were include: ESR, C-reactive protein (CRP), Rheumatoid factor (RF) and serum uric acid. A pre-tested questionnaire was designed to obtain information from both patients and control group about past medical and drug history.

About five milliliters of venous blood was aspirated using disposable syringes and needles. Samples were collected between 09.00-12.00 Am. The blood was allowed to clot in plain tubes for 15 minutes, serum was obtained by centrifugation at 3000 rpm for 10 minutes and transferred into plain plastic tubes and kept frozen at (-20) C° until the time of assay

Measurement of IL-6 in serum: The IL-6 Enzyme immunoassay kit provides materials for the quantitative determination of IL-6 in serum and plasma. This assay is intended for in vitro diagnostic use only. The IL-6 was measured using a solid phase enzyme-linked immune-sorbent assay (ELISA) based on the sandwich principle (Figure 1).

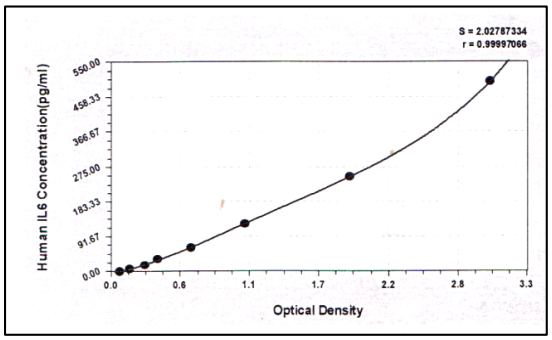


Figure 1. Standard Curve of IL-6 (pg/ml)

Cusabio - China Human IL-6 ELISA Kit was used to determine serum IL-6 level in this study. Normal values: 0.4-2.1 Pg/ml

The BMI was measured in this study according to world health organization (WHO) equation (weight / (hight)²)

The bone minerals density (BMD) was measured by DXA scan in Al-Yarmouk Teaching Hospital (Dexxum3-Korea Company) for both cases and controls.

The results were presented as sample size (n),mean ± standard deviation (SD) .the statistical significance of difference in mean between two groups was analyzed by student t-test. P-value < 0.05 was considered statistically significant.

All statistical analyses were done using IBMSPSS version 21 computer software (Statistical Packages for Social Sciences).

RESULT

Study showed significant increase of BMI in patients (mean ± SD) (31.6 ± 8.7) when compared to controls (mean ± SD) (26.2 ± 3.6) , P-value < 0.05. (Table-1) (Figure-2).Also this study showed significant increase of IL-6 level in patients mean (± SD) (3.2 ± 2.2) when compared to controls (mean ± SD) (1.6 ± 0.9) P-value < 0.05 . (Table 1) (Figure-3).Also this study showed significant decrease of BMD level in patients (mean ± SD) (-2.2 ± -1.1) when compared to controls (mean ± SD) (-0.7 ± -0.6), P-value < 0.05 . (Table-1) (Figure-4).

Table 1. Comparison of BMI and serum IL-6 in NOA patients with controls

Variable	NOA Patients	Controls	P- value
Number	60	60	
BMI (Kg/m2)			<0.05*
(Mean ± SD)	31.6 ± 8.7	26.2 ± 3.6	
IL-6 (Pg/ml)			<0.05*
(Mean ±SD)	3.2 ± 2.2	1.6 ± 0.9	
BMD(t-score)			<0.05*
(Mean ±SD)	-2.2 ± -1.1	-0.7 ± -0.6	

*** Significant differences**

Figure 3: Comparison of BMI (mean ± SD) Between Controls and NOA Patients.

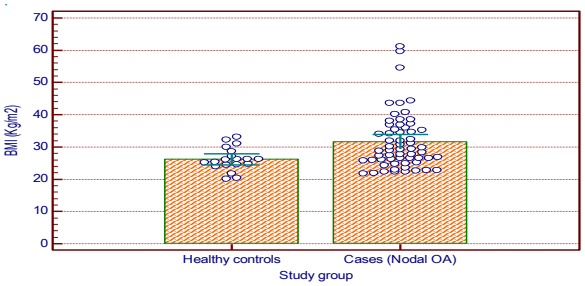
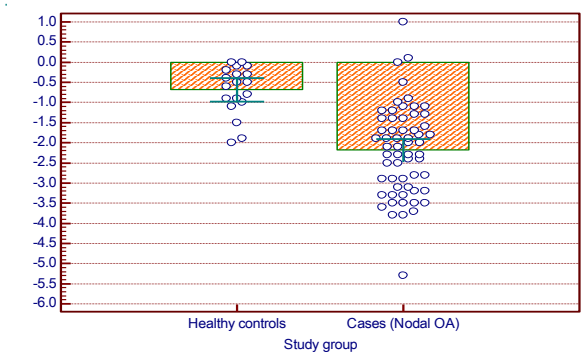


Figure 4: Comparison of Bone Mineral Density (BMD) (bone t-score) (mean ± SD) between controls and Nodal Osteoarthritis(NOA) patients



DISCUSSION

This study shows a significant increase of body mass index(BMI) between patients and controls this study agree with (Lauren , et al. 2013) who found that the patho-physiology of obesity-related OA is likely to be multi-factorial (9).

Structural joint damage is thought to result from both mechanical factors, including increased forces about the joint, decreased muscle strength and altered biomechanics during every day activities and metabolic factors, as being obese also increases the risk of OA in non weight-bearing joints such as the hands because the NOA consider as later status for OA (10).

But the study was disagree with (Raid , et al .2009) who found no associated changes between BMI in the cases and controls, but they proved the association between BMI and inflammatory hormones (like adipokinse as adiponectin and leptin)(11).

There are two methods show the relationship between bone mineral density(BMD) and OA generally and NOA specially, these are genetic and metabolic , because the two diseases occur in old age(12,13).

The genetic method shows relationship between OA and BMD by known gene responsible for OA and decrease BMD and bone turnover. (Tim , et al .2004) have proved this correlation (13). This proved when found urinary collagen cross links (markers of bone resorption) is due to share genes for two diseases (12).

The metabolic method shows the relationship between BMD and NOA as there is a correlation of sex hormones and turnover of bone. there are various studies about this subject, (Burger , et al .1996) shows that BMD increase for patients with general OA or NOA but after 60 years age the BMD decreases (13), (Valentina Živković , et al .2010) shows that at postmenopausal period the BMD decrease (14), (Abir Naguib, et al 2011) also shows that with age the bone turnover increase due to increase of urinary deoxypyridinoline (DPD) (16). This three studies supported the results of this study because our cases have age 60 years and more, also all the females in this study are postmenopausal (13, 14, 15).

This study shows significant increase of serum IL-6 in NOA patients when compared with controls. This difference is due to that all the NOA cases are postmenopausal, estrogen hormone decrease physiologically at this condition lead to error at bone formation because Osteoclast apoptosis is regulated by estrogens (16).

With estrogen deficiency, the osteoclasts live longer and are therefore able to absorb more bone and this will promote increase IL-6 level because interleukin 6 is a potent stimulator of bone resorption, and estrogen blocks the osteoblasts synthesis of interleukin- 6(16).

Estrogen may also antagonize the interleukin- 6 receptors, this lead to decrease osteocalcin then a decrease of BMD and the appearance of urinary deoxypyridinoline (DPD) (17).

This results agree with (Abir Naguib, et al 2011) who proved that the relationship between NOA ,bone turnover and urinary DPD (15). IL- 6 can be an important mediator in increased bone resorption of NOA patient because it mediated the inflammation in joints this agree with (Dequeker , et al .2003)(17).

Conclusion

This study proved the role IL-6 as inflammatory mediator in NOA patients, and BMI have a role in status of increased Interleukin-6 in NOA patients, as well as a relationship between NOA disease and decrease of BMD in elderly women.

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