ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 13, Issue, 01, pp.15998-16000, January, 2021

DOI: https://doi.org/10.24941/ijcr.40709.01.2021

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF INTERLEUKIN-1 BETA (IL-1β) AND ALKALINE PHOSPHATASE (ALP) IN POST MENOPAUSAL KNEE OSTEOARTHRITIC FEMALE PATIENTS

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ARTICLE INFO

Article History:
Received 24th October, 2020
Received in revised form
24th November, 2020
Accepted 18th December, 2020
Published online 30th January, 2021

Key Words:

Osteoarthritis.
Interleukin 1-Beta,
Alkaline Phosphatase.

ABSTRACT

Background: Osteoarthritis (OA) is one of the most common forms of arthritis. It gets worse as the disease progress and leads to chronic pain, stiffness as well as reduced mobility of joints. There are many attributable risk factors like gender, advancing age, obesity as well as mechanical factors. The pathology of the disease is characterized by cartilage destruction, inflammation of synovial membranes causing weak muscular strength. There are many specific and sensitive biomarkers for OA which may be helpful in the management of the disease. **Objective:** The objective of the study was to highlight the role of several biomarkers like Interleukin-1 Beta (IL-1β) and Alkaline Phosphatase (ALP) in post menopausal knee osteoarthritic female patients. **Material & Methods:** The present study was carried out in 200 female subjects of the age group of 45-70 years out of which 100 postmenopausal females without osteoarthritis and 100 were knee osteoarthritis diagnosed postmenopausal patients were selected. The blood samples were collected from department of Orthopedics of UPUMS, Saifai, Etawah, and then the serum levels of Interleukin 1 Beta and Alkaline Phosphatase was measured. **Results:** IL-1β was significantly increased ($P<0.001$) and ALP was also increased ($P<0.05$), in female patients with knee osteoarthritic as compare to the control group. Also, the correlation is made between IL-1β and ALP and a negative correlation ($r<0.0791$) obtained in osteoarthritic female patients. **Conclusion:** The result of our study shows that the biochemical parameters IL-1β play a more significant role than the Alkaline Phosphatase in the development of osteoarthritis disease in post menopausal knee osteoarthritic female patients.

Citation: ***Kumar Vivek Anand, Pradeep Sharma, Sunil Kumar, Kalbe Jawad, Ajai Kumar, Prem Prakash Bharti and Mimoh Sharma. 2021*** "Role of Interleukin-1 Beta (IL-1β) and Alkaline Phosphatase (ALP) in post menopausal knee osteoarthritic female patients", *International Journal of Current Research*, 13, (01), 15998-16000.

INTRODUCTION

Osteoarthritis (OA) is the most common type of arthritis and causing disability and discomfort in older adults. It is a chronic, progressive, subtle loss of articular cartilage leading to pain, inflammation, and disability. The disease primarily affects the knee, wrist, feet, and spine. The disease is widely prevalent both in developed and developing countries. The incidence of OA in our country India ranges from 22% to 39 % (Osteoarthritis, 2021). Generally, it affects more women than men and in particular those who have attained menopause. The detailed pathological analysis of OA reveals cartilage degradation of joints, thickening of subchondral bone, and inflammation of the synovial membranes (Roman-Blas, 2009).

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Furthermore, the disease progresses to subsequent stages characterized by the proteolytic breakdown of the cartilage matrix leading to disruption of chondrocytes metabolism causing increase secretion of degradative enzymes such as collagenases and aggrecanases**.** ***Furthermore,*** the next stages involve fibrillation and erosion of the cartilage surface and ultimately leading to the production of inflammatory cytokines and proteases (Nguyen, 2017). Biomarkers are, first of all, molecules of connective tissue matrices that are released into biological fluid during the process of tissue turnover. Therefore, it is crucially important to identify the specific and sensitive biomarkers which truly reflect abnormalities of the bone, cartilage, and synovium tissue turnover for monitoring OA, but on the contrary, they are still in process of achieving the said aim (Rousseau, 2007). It is noteworthy that out of several biochemical markers of OA which have been proposed corresponding to criteria of the BIPED classification (Elsaid, 2006; Qvist, 2010), they have been recently created to provide a common language related to OA biomarkers for both clinical

and research applications (Bauer, 2006). During the pathogenesis, the precursor of IL-1β, pro-IL-1β is produced and matures (Daheshia, 2008). The articular resident cells of joint tissue produce some amount of IL-1β and on analysis, it was found markedly increased in the chondrocytes (Pelletier, 1995). Additionally, it is evident from studies that apart from increased degradation of ECM, IL-1β can decrease ECM synthesis by decreasing the anabolic activities of chondrocytes or the cell densities of articular cartilage. The IL-1β blockade is a potential way to manage OA pathology. Also, almost every current treatment for OA has shown some degree of a decrease in the level of IL-1β or interference with the downstream effects of IL-1β. OA treatments that interfere with the effects of IL-1β are steroids, nonsteroidal anti-inflammatory drugs (NSAID), Hyaluronic acid, Glucosamine, analgesics such as Morphine, and exercise and weight loss.

Additionally, it has been found that different biochemical markers were indicative of bone turnover in animal models and humans. Concentrations of proactive and active metalloproteinase, alkaline phosphatase (ALP), and subchondral bone turnover were found to markedly increase in subchondral bone specimens obtained from patients with OA. Osteoarthritis affects all biomechanical dynamics of the joints, ultimately leading to functional failure. Alkaline Phosphatase (ALP) is a hydrolase enzyme that removes the phosphate groups from molecules such as nucleotides, proteins, etc. The ALP is a byproduct of osteoblastic activity (Rodan). Hence, the objective of the present study was to investigate the role of bone-specific alkaline phosphatase (BALP) in patients with symptomatic knee OA. Therefore, in conclusion, the present study may help us to understand the comparative roles in the development of knee osteoarthritis in postmenopausal females.

MATERIALS AND METHODS

The study protocol was evaluated by the Institutional Ethical Committee of UPUMS, Saifai, Etawah. Before the enrolment of the study, written informed consent from each subject was obtained in response to a fully written and verbal explanation of the nature of the study. The present study was carried out in 200 female subjects of the age group of 45-70 years suffering from OA out of which 100 were postmenopausal females without osteoarthritis and 100 were knee osteoarthritis diagnosed postmenopausal patients. The blood samples of about 5 ml were collected from patients attending the Orthopedic Out Patient Department of UPUMS, Saifai, Etawah. Then, the blood samples were centrifuged at 5000 minutes for 5 minutes, and then the obtained serum was stored at – 20 °C until they were analyzed. The serum level of Interleukin-1 Beta and ALP was analyzed by Boster Elisa Kit and colorimetric enzymatic method respectively in the Department of Biochemistry, UPUMS, Saifai, Etawah. The results were analyzed statistically using chi-square and spearman coefficient tests.

RESULTS

Table-1 shows the status of IL-1β and ALP in osteoarthritic female patients and the control group respectively. IL-1β was highly significantly associated with female patients with knee osteoarthritic as compared to the control group ($P<0.001$).

Additionally, Table-2 shows a negative correlation between IL-1β and ALP in postmenopausal knee osteoarthritic female group ($r<0.791$).

DISCUSSION

Osteoarthritis (OA) is one of the chronic diseases which are characterized by inflammation of joints as well as erosion of cartilages. There are vivid risk factors like aging, obesity, muscle weakness, and injury of joints related to occupation or sports activities, etc. (Sen, 2020). In India, it was observed that the urban population has a higher incidence (5.5%) than the rural population (3.3%). But, after adjustment in age and sex distribution, a higher prevalence was observed in rural communities (Haq, 2011). In recent years, it has been found that different biochemical markers were indicative of bone turnover in animal models as well as in humans. Also, various studies show that these biochemical markers are sensitive to alterations in the bone turnover rate (Paker, 2011).

Therefore, these markers can be measured in the serum or urine and they may provide crucial information regarding the formation and destruction of the bone. Serum IL-1β**,** one of the enzyme biochemical markers in our study was found to be significantly ($p=0.001$) higher among cases 187.59±26.89 pg/ml compared to controls 120.9±16.9 pg/ml (Table-1). These values corresponded to several studies, out of which one was led by Xu Yang et al. (Yang, 2016) in which they studied the Mechanical and IL1β response of miR-365 and its contribution to OA development by targeting Histone Deacetylase 4 and the team observed that IL-1β is an important catabolic factor of joint inflammation and cartilage degradation in OA. In the same study, they investigated whether the expression of miR-365 was induced by IL1β and found that primary human chondrocytes were stimulated with IL-1β for 24 hours. Also, they found that IL1β stimulation of chondrocytes leads to significant up-regulation of miR-365 expression.

Another biochemical marker of our study was Serum ALP, unlike wise previous biomarkers in the study it was found to be less significant ($p=0.05$) but higher among cases (287.03±54.99 U/L) compared to controls (114.9±52.26 U/L) (Table-1). However, another study conducted by Qazi Najeeb (Najeeb, 2015) studied the comparison of alkaline phosphatase, lactate dehydrogenase, and acid phosphatase levels in Serum and Synovial Fluid in patients with OA and found serum ALP level mean 83.6 ± 15.0IU/L.

In their study, they found that in an inflammatory disease like OA, ALP level in serum doesn't change much may be due to the absence of a chemical signal. Furthermore, the above results forced us to think about whether all these parameters are closely related to each other. Therefore, we made correlation studies between these biomarkers and found a negative significant correlation between serum IL-1β and ALP ($r = 0.791$). Therefore, the above results forced us to postulate that IL-1β plays a more important role than ALP in the development of OA. Additionally, IL-1β could be taken as a suggestive & more reliable marker than ALP for assessment of the onset of osteoarthritis.

Table 1. Status of IL-1β and ALP in normal healthy female control and postmenopausal knee osteoarthritic female

Normal healthy control female subjects (n= 100)		IL-1β (pg/ml)	ALP (U/L)
	Min.	5.6	51
	Max.	196.41	135
	Mean±SD	120.9±16.9	114.9±52.26
	SE	1.369	9.226
Postmenopausal knee osteoarthritic female subjects (n=100)	Min.	251.8	150
	Max.	416.2	539
	Mean±SD	187.59±26.89	287.03±54.99
	SE	4.6	17.49
p value (of cases and controls)		0.001*	0.05**

***** Value expressed as a (P<0.001) significant in IL-1β ******Value expressed as a (P<0.05) not significant in ALP

Table 2. Correlation of IL-1β and ALP in Postmenopausal Knee Osteoarthritic female subjects

VARIABLES	IL-1β (pg/ml)	ALP (U/L)
IL-1β	-	.791 **
		Sig (2 tailed) = 0.05

** Value expressed as a (r<0.05) Significant

Conclusion

The present study shows that the Interleukin-1 Beta and ALP are important contributing biomarkers in causing knee joint Osteoarthritis in post menopausal females. However, in these biomarkers, Interleukin 1 Beta has a more specific and significant role in the development of OA. Therefore, conclusive to the discussion above, we may say that the estimation of IL-1β biomarker has a more important role in the development of OA and can guide us better in the diagnosis and treatment of osteoarthritis. Furthermore, extended studies are needed to further delineate their role as biomarkers and in the development of personalized approaches in disease prevention and management.

Glossary Abbreviations

ALP: Alkaline Phosphatase
BIPED: Burden of Disease, Investigative, Prognostic, Efficacy of Intervention and Diagnostic
BALP: Bone specific Alkaline Phosphatase
ECM: Extra Cellular Matrix
IL-1β: Interleukin 1-Beta
OA: Osteo Arthritis

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