

# Synovial Fluid Alkaline Phosphatase Levels of Knee Joint in Osteoarthritis

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## ABSTRACT

OA of knee is a major problem worldwide. Biochemical markers might be of help in prevention, diagnosis, prognosis or treatment. Synovial fluid was collected from knee joint of 129 OA cases and 116 controls, and assayed for ALP. Concentration of AP in synovial fluid was significantly higher in cases than controls. The present study results point toward using ALP estimation as an important, potential parameter for OA. As the findings demonstrate an increase in ALP, the pathogenesis of OA should be further investigated, and other similar biological parameters should also be assessed.

**Keywords:** osteoarthritis, knee joint, synovial fluid, alkaline phosphatase

## INTRODUCTION

Osteoarthritis (OA) is a major source of pain, disability, and socioeconomic cost worldwide. <sup>(1)</sup> Knee OA is a major public health issue because it causes chronic pain, reduces physical function and diminishes quality of life. Ageing of the population and increased global prevalence of obesity are anticipated to dramatically increase the prevalence of knee OA and its associated impairments. <sup>(2)</sup> Patients with OA are at a higher risk of death compared with the general population. <sup>(3)</sup>

Importantly, the symptoms are often associated with significant functional impairment, as well as signs and symptoms of inflammation, including pain, stiffness and loss of mobility. <sup>(4)</sup> Joint replacement is an effective treatment for symptomatic end-stage disease, although functional outcomes

can be poor and the lifespan of prostheses is limited. Consequently, the focus is shifting to disease prevention. This task is challenging since conventional imaging techniques can detect only quite advanced disease and the relation between pain and structural degeneration is not close. <sup>(1)</sup> Thus, biochemical markers might be of help in prevention, diagnosis, prognosis or treatment.

The epidemiology of the disorder is complex and multifactorial, with genetic, biological, and biomechanical components. Etiological factors are also joint specific. <sup>(1)</sup> Catabolic and proinflammatory mediators such as cytokines, nitric oxide, prostaglandin E<sub>2</sub> and neuropeptides are produced by the inflamed synovium and alter the balance of cartilage matrix degradation and repair, leading to excess production of the proteolytic enzymes responsible for cartilage breakdown. <sup>(5)</sup> Intriguing is the role of growth factors such as TGF- $\beta$ , IFG, BMP, NGF, and others, which do not simply repair the tissue damage induced by catabolic factors, but play an important role in OA pathogenesis. <sup>(6)</sup> Other factors including enzymes might also be involved in this process. Livne et al found that in degenerating articular cartilage of OA cases, alkaline phosphatase (ALP) activity was increased. <sup>(7)</sup>

With this background the authors thought to investigate the concentration of AP in synovial fluid of the knee joint in OA cases.

## MATERIALS AND METHODS

The study was a hospital-based case-control study conducted in a tertiary care center in West Bengal, India. The study was approved by the Institutional Ethical Committee. Before enrolment of the subjects, informed consent was obtained from all the participants. The duration of the present study was 9 months and included 129 OA patients attending the Orthopedics outpatient department (OPD) during the above mentioned period. These patients were further grouped into 42 younger (<60 years of age) and 87 older patients (more than 60 years of age). 116 age- and sex-matched patients attending OPD, characterized by the absence of any sign of and of personal or family history of OA, served as controls. Consecutive patients attending the OPD and satisfying inclusion criteria were selected assuming that the patients attended OPD randomly. Exclusion criteria included participants who had coexisting diseases of knee joint. Complete history and physical examination of all cases and controls were undertaken.

Synovial fluid was collected from each case and control. All samples were coded and assayed in a blind fashion by an investigator who was unaware of the participant's clinical status. ALP levels were assayed by PNPP method. Statistical analysis of data was performed using SPSS software version 20 (IBM, New York, USA), and inferences were drawn. A value of  $p < 0.05$  was considered to be statistically significant and  $p < 0.001$  highly significant.

## RESULTS

Table 1. Synovial fluid alkaline phosphatase levels (IU/L) in subjects expressed as Mean + SD.

	Controls	Group 1	Group 2
Levels	94+19	102+17	118+23

### t-test results

Between controls and group 1:

p value and statistical significance:

The two-tailed p value equals 0.0175

By conventional criteria, this difference is considered to be statistically significant.

Confidence interval:

The mean of control minus Group 1 equals -8.00

95% confidence interval of this difference:  
From -14.58 to -1.42

Intermediate values used in calculations:

$t = 2.4019$

$df = 156$

standard error of difference = 3.331

SEM for controls and group 1 are respectively 1.76 and 2.62

Between controls and group 2:

p value and statistical significance:

The two-tailed p value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:

The mean of control minus Group 2 equals -24.00

95% confidence interval of this difference:  
From -29.82 to -18.18

Intermediate values used in calculations:

$t = 8.1333$

$df = 201$

standard error of difference = 2.951

SEM for controls and group 2 are respectively 1.76 and 2.47

## DISCUSSION

In OA there is progressive loss of articular cartilage, increased subchondral plate thickness, formation of new bone at the joint margins and subchondral bone cysts.<sup>(8)</sup> Also, there is a remnant of calcified cartilage at the junction of the articular hyaline cartilage and adjacent subchondral bone. Gradually, there is vascular invasion, and this zone of calcified cartilage advances into the articular cartilage, that leads to a decrease in articular cartilage thickness.<sup>(9)</sup> These structural alterations in the articular cartilage and periarticular bone lead to change of the adjacent articulating surfaces.<sup>(10)</sup> Along with these changes, there are alterations in subchondral bone remodeling, which ultimately produces an adverse biomechanical environment and increases articular cartilage deterioration.<sup>(11)</sup>

Osteoblasts are responsible for the synthesis and mineralization of bone during both initial bone formation and later bone remodeling; osteoblasts produce fibronectin required for bone matrix formation. <sup>(12)</sup> Recently a hypothesis has been put forward that states that abnormal OA osteoblasts directly influence cartilage metabolism. Westacott et al showed that conditioned media from primary osteoblasts of OA patients significantly altered glycosaminoglycan release from normal cartilage in vivo, while cytokine release from these cells remained intact. <sup>(13)</sup> These findings may be due to the following: Hilal et al reported that in vitro primary cultures of osteoblasts from human OA subchondral bone have an altered phenotype, and that the plasminogen activator (urokinase)/plasmin system activity and IGF-1 levels are elevated in these cells. <sup>(14)</sup>

Bone, and especially the subchondral bone plate, is involved in the pathogenesis of osteoarthritis (OA). OA bone tissue is sclerotic yet undermineralized indicating abnormal bone cell metabolism. Some specific pathways involved in sequence of changes leading to OA have been investigated, and indeed are modified in OA subchondral osteoblasts. Subchondral bone sclerosis in OA may be due to abnormal osteoblasts characterized by increased metabolic activities that result in an increase in osteoid matrix that is undermineralized. *In vitro* alkaline phosphatase activity of human osteoblasts isolated from the subchondral bone plate of tibial plateaus have been found to be higher in cells from OA patients than in those from normal individuals. <sup>(15)</sup> Alkaline phosphatase was also significantly elevated in OA hip bone. <sup>(16)</sup> In the present study also concentration of AP in synovial fluid of the knee joint in group 1 was significantly higher, and the corresponding values in group 2 were highly significantly higher, than controls (table 1).

This study has limitations that should be considered. To assess ALP, PNPP method was used. ALP can be estimated by

various methods, but the present method was employed as it was standard and time-tested. Patients were taking a number of medications to control OA. However, these treatments are characteristic of patients with OA and do not affect serum ALP levels. Furthermore, the number of patients in the study group was not large. Thus, care should be taken while extrapolating the present findings to other populations. We conducted the present study in a tertiary care hospital. However, in our country, most people visit district, subdivisional, and lower-tier hospitals for treatment. Hence, results of our study might not reflect the true picture of the population as a whole. Probably, a multicentric study on a larger population would be better in revealing the actual statistics. Despite these limitations, we believe that our study results point toward using ALP estimation as an important, potential parameter for AD. As our findings point to an increase in ALP, the pathogenesis of OA should be further investigated, and other similar biological parameters should also be assessed.

## CONCLUSIONS

In the present study, AP in synovial fluid of the knee joint was significantly higher in OA than controls. Still, to confirm the findings, further research on a larger population with a multicentric study should be carried out.

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