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Original Article

A Comparative study on Serum ALP, LDH & Acid Phosphatase Levels with Patients suffering from Rheumatoid Arthritis and Osteoarthritis

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ABSTRACT

Pain and swelling in joints is a fundamental feature of Rheumatoid Arthritis (RA),it is a chronic multisystem disease of unknown cause. Osteoarthritis (OA) has been characterized by progressive articular cartilage loss and osteophyte formation. This study was undertaken to evaluate whether it is possible to distinguish OA from RA by comparing LDH, ALP, Uric Acid and ACP levels within the synovial fluid and the serum. This was a cross sectional study, total of 317 cases were included out of which 172 cases were already diagnosed cases of having OA and 145 cases were diagnosed with RA. Joint fluid was obtained by arthrocentesis from patients with clinical evidence of knee arthritis and joint effusion, blood samples were taken from the same patients. A combination of serological and aspiration analyses was done. The mean levels of synovial LDH, ALP, ACP in RA patients were 474.23 ± 83.01 mg/dL,108.23± 54.43IU/L, 10.5±8.5 IU/L and in OA group were 311.86 ± 153.91 mg/dL,83.6 ± 15.0IU/L, 3.7±1.8 IU/L respectively, there was a statistically significant difference between them ($p<0.0001$). In RA patients, the synovial fluid levels of ALP with LDH ($r=0.6549$) showed direct and stronger correlation than the correlation between synovial fluid levels of ACP with LDH and ALP ($r=0.4182$ and $r=0.4147$) respectively. An assay for synovial fluid ALP, LDH and ACP levels may serve as a simple method for diagnosing and differentiating RA from OA in the future and this may allow for more targeted pharmaceutical and surgical intervention.

Keywords: Rheumatoid Arthritis, Osteoarthritis, LDH, ALP, ACP

INTRODUCTION

Pain and swelling in joints is a fundamental feature of Rheumatoid Arthritis (RA), it is a chronic multisystem disease of unknown cause. The characteristic feature of RA is persistent inflammatory synovitis, usually involving peripheral joints.[1] Synovial fluid analysis is commonly used to diagnose arthritis and to evaluate the inflammatory activity of joint effusions, it may also be of help in predicting the outcome of joint inflammation.[2] Osteoarthritis (OA) has been characterized by progressive articular cartilage loss and osteophyte formation. Although OA was long considered to be due only to an imbalance between loss of cartilage and an attempt to repair cartilage matrix, it is now known that OA, at least in the knee, is a heterogeneous disease involving all the articular tissues including cartilage, subchondral bone, menisci, and periarticular soft tissues such as the synovial membrane. Synovitis is often present and is considered to be secondary to the alterations in other joint tissues. Yet, findings indicate that synovial inflammation could be a component of even the early events leading to the clinical stage of the disease.[3,4]

Alkaline phosphatase (ALP) is an enzyme which is active in the process of bone formation where it catalyzes a chemical reaction that removes a phosphorus molecule and removal of the phosphorus enables the deposition of calcium in the newly formed bone. Since it is found localized in the plasma membrane of the osteoblastic cells, its role in bone mineralization is justified, increased concentration of serum ALP is a common feature in RA, although its origin remains unclear. [5,6] Lactate dehydrogenase (LDH) is an enzyme that is expressed at higher levels when cells are distressed and damaged. Elevating LDH is a possible indication of disease progression. [7] According to different studies, increases in Acid Phosphatase (ACP) activity in synovial fluid have a close

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relationship with activity of underlying disease and can show the degree of inflammation in joints. [8] So the study was undertaken to evaluate whether it is possible to distinguish OA from RA by comparing LDH, ALP, Uric Acid and ACP levels within the synovial fluid and the serum.

MATERIALS AND METHODS

This cross sectional study with a total of 317 cases were included out of which 172 cases were already diagnosed cases of having OA and 145 cases were diagnosed with RA. The cases were patients who attended the outpatient clinic in the Department of Orthopaedics. Informed and written consent was obtained from all the patients. Joint fluid was obtained by arthrocentesis from patients with clinical evidence of knee arthritis and joint effusion, blood samples were taken from the same patients. The arthritis was diagnosed as RA and OA based on physical examination, laboratory results and radiological findings. Synovial fluid was collected in sterile plain tubes and was centrifuged with the speed of 1500 rpm. Supernatant was used for biochemical analysis and to determine the number of white blood cells. Blood was collected in a red top vial and was centrifuged to separate serum from it. A combination of serological and aspiration analyses was done for LDH by modified IFCC method, ALP by IFCC method, Uric Acid by Uricase method, ACP by Modified King's method, glucose by GOD-POD method and proteins by Biuret method and these parameters were compared between OA and RA cases. All these parameters were analysed on autoanalyser (Transasia Chem 7) and were immediately analysed for biochemical parameters under study. Means ± standard deviation were calculated and student t-test was applied to find out significance level. Statistical significance was defined as two-tailed $p<0.05$ for all tests unless otherwise specified. Pearson correlation test was used to find the correlation.

RESULTS

The mean age of patients in RA group was 51 ± 8.6 years (ranging from 44-60 years) and in OA group it was 55 ± 11.6 years (ranging from 44-67).Cell counts of all synovial samples were examined to rule out the presence of infectious causes. Cell counts of synovial fluids were 100-1800 WBC/mL and 1400-35000 WBC/mL in OA and RA groups, respectively. But none of them were in boundary of infected arthritis. The mean levels of synovial LDH, ALP, ACP in RA patients were 474.23 ± 83.01 mg/dL,108.23 ± 54.43IU/L, 10.5±8.5 IU/L and in OA group were 311.86 ± 153.91 mg/dL,83.6 ± 15.0IU/L, 3.7±1.8 IU/L respectively, there was a statistically significant difference between them ($p<0.0001$). Synovial Uric Acid, glucose and protein levels in RA were 3.72 ± 1.59 mg/dL, 64.01 ± 9.05 mg/dL and 4.5± 1.5 gm/dL and in OA were 4.13 ± 1.70 mg/dL, 75.0 ± 19.0 mg/dL and3.7 ±0.5gm/dL respectively, statistically insignificant (>0.05) Table-1. Also, the mean levels of serum LDH, ALP and ACP were192.67 ± 56.54 mg/dL, 245.2 ± 91.2 IU/L and 6.79 ± 4.75IU/L in RA cases and 107.91± 9.77 mg/dL, 192.3 ± 45.2IU/L and 4.81 ± 1.02IU/L in OA cases, respectively and there were significant difference between the two (<0.0001), the Uric Acid levels between RA and OA were 6.43 ± 1.75mg/dL and 5.23 ±1.55 mg/dL respectively, these were statistically insignificant (>0.05) Table-2. In RA patients, the synovial fluid levels of ALP with LDH (r=0.6549) showed direct and stronger correlation than the correlation between synovial fluid levels of ACP with LDH and ALP (r=0.4182 and r=0.4147) respectively (Figure-1, 2 and 3).

DISCUSSION

Considering the chronic course of RA and not completely known pathology of the disease and the destructive debilitating nature of RA, it is important to determine the level of inflammation. Therefore, due to non-specific clinical features and insufficient diagnostic tests, competency of synovial fluid ALP for diagnosing RA was evaluated in this study. According to previous studies, serum ALP level and average of synovial fluid ALP are different among Asian countries. But none of studies had determined used ALP as marker distinguishing between RA and OA.[9] Our results showed that the average level of serum and synovial fluid ALP have statistically significant difference between RA and OA. Furthermore, synovial fluid ALP can be used as an appropriate screening test for diagnosing Rheumatoidjoint effusions. The reason for raised ALP levels in synovial fluid and/or serum in RA can be explained as bones that are attacked by the immune system in RA is flooded by chemical signals of inflammation. These signals attempt to rebuild the bone and an elevation in ALP is seen. Non-inflammatory arthritis like OA does not have the chemical signals that occur with inflammatory arthritis and as such, there is not an elevation in ALP levels.[10]

LDH is an enzyme that helps facilitate the process of turning sugar into energy for cells to use. In inflammatory conditions like RA, LDH may be released into the bloodstream causing the levels to increase and higher levels of LDH in the blood indicate acute or chronic cell damage. Veys et al had shown that cases of rheumatoid arthritis had high LDH activity both in cell-free fluid and in cellular material. RA patients had an increased

percentage of LDH in the serum and in synovial effusions as compared to OA, this was in concordance with the present study.[11] In another study it was noted thatthere was a difference in synovial fluid LDH levels between RA and OA patients andthere was significant difference between serum LDH levels in OA patients when compared with normal healthy individuals.[12] Serum and synovial ACP levels were significantly higher in RA patients when compared with OA patients, reason can be explained as in the case of patients of RA, joints lysosomes lining cells might release their contained hydrolytic enzymes into the synovial fluid causing the increase in ACP levels.[13]

The correlation coefficient between ALP and LDH is stronger than the correlation coefficient between ACP with ALP and LDH; however extensive search did not reveal any literature mentioning the correlation between them. So it can be emphasized that ALP and LDH levels in synovial fluid showed significant increase in RA patients and these can be used to differentiate RA with other types of arthritis. By measuring LDH, ALP and ACP in joint fluid rather than in blood serum appears to result in a test with higher diagnostic accuracy. Moreover, because these parameters does not include in the routine clinical measurement, widespread adaptation of these tests would be fairly straightforward.

CONCLUSION

These new biomarkers were significantly elevated in RA synovial fluid in comparison with OA. In addition, significant elevation was not limited to the synovial fluid as a whole, but also occurred in serum as well. Identified biomarkers may prove useful for diagnosis or differential diagnosis of RA patients, as well as for stratification and monitoring of patients in routine or experimental clinical trials.

Table 1: Depicting Mean, Standard Deviation and Significance In Serum differentiating RA from OA

Parameters	OA (n=145)	RA (n=172)	p-value
Serum LDH (mg/dL)	107.91± 9.77	192.67 ± 56.54	< 0.0001
Serum ALP (IU/L)	192.3 ± 45.2	245.2 ± 91.2	< 0.0001
Serum Uric Acid (mg/dL)	5.23 ±1.55	6.43 ± 1.75	>0.05
Serum ACP (IU/L)	4.81 ± 1.02	6.79 ± 4.75	< 0.0001

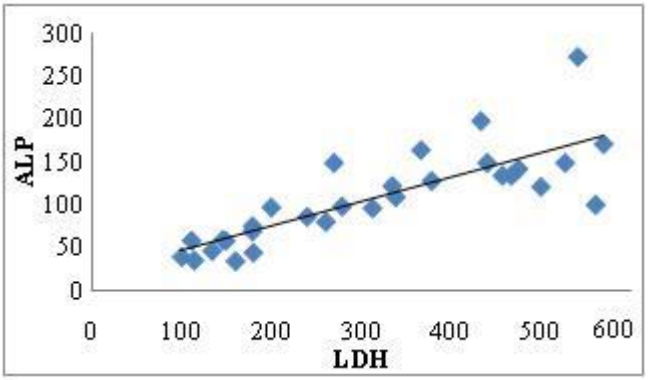

Figure 1: Showing Correlation between Synovial Fluid LDH &Alp Levels in RA Patients

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