Activity of Serum Alkaline Phosphatase in Rheumatoid Arthritis for Diagnosis and Management

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ABSTRACT
Purpose: The present study examines the Activity of Serum Alkaline Phosphatase in Rheumatoid Arthritis for diagnosis and management.
Methods: A total number of 100 subjects were selected from orthopaedics OPD at CCM Medical College Hospital Durg. 58 subjects are suffering from Rheumatoid Arthritis age range of 45 to 70 years. 42 subjects age, sex matched was selected for control group. Controls were clinically and physically normal and healthy.
Results: The level of alkaline phosphatase statically significantly higher in Rheumatoid arthritis patients than normal healthy control group. When Values are compared with normal control values 15 male patients out of 23 patients ALP level was highly increased found while out of 35 female patients 26 female patients ALP level highly increased found than normal healthy controls. Increased level of ALP indicates that the disease is more active.
Conclusion: Increased level of ALP indicates that the disease is more active. The increased activity of ALP may be due to its leakage from injured or killed cells. Our study will provide in clinical practice to use the easy and least expensive test, to assess the disease and response to treatment. Very high concentrations of serum alkaline phosphatase may indicate an underlying secondary disease.

Keywords: Rheumatoid Arthritis (RA), Alkaline Phosphatase (ALP), Osteoporosis, Osteocalcin, Placental Alkaline Phosphatase (PALP).

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INTRODUCTION
Alkaline Phosphatase (ALP) comprises a group of enzymes that catalyze the hydrolysis of phosphate esters in an alkaline environment, generating an organic radical and inorganic phosphate. Like other enzymes, LDH has many isoenzymes. In healthy adults, this enzyme is mainly derived from the liver, bone and lesser amounts from intestines, placenta, kidneys and leukocytes. Liver, Bone, and Placenta are primary sources of ALP. An ALP in normal adult serum is primarily derived from the liver or biliary tract. Elevation of ALP is seen in primary or secondary liver cancer. Quantifications are helpful in evaluating metastatic cancer with bone or liver involvement. Placental alkaline phosphatase (PALP) is synthesized by the trophoblast and is elevated circulation of pregnant mothers. Serum ALP levels are frequently elevated in patients with multiple cancers, variety of diseases, such as Rheumatoid Arthritis extra hepatic bile obstruction, intrahepatic cholestasis, infiltrative liver disease and hepatitis. There are reports and pilot studies suggesting that the elevated ALP can aid in detection of metastatic liver disease. This is an important issue as biological detection of liver metastases represents an important factor in the prognosis of patients with stomach cancer and it is useful in detection of bone metastasis. Biochemical marker of bone turnover is Alkaline phosphatase provides clinically useful evidence of the normal and pathologic process that reflect bone cell activity on the skeleton. Standing the variety of biochemical markers that reflect the activity of osteoblasts and Osteoblasts Alkaline phosphatase introduced in to clinical practice in 1929, was the first biochemical marker of bone turnover and it is still the best most widely used clinical marker in our study to aid in managing patients with a variety of skeletal disorders. We discussed those disorders. Alkaline Phosphatase is found in the plasma membrane of Osteoblasts and in cells of the liver, kidney, intestine, spleen and placenta. In generally bone formation markers are measured in serum and reabsorption are measured in urine or serum. So in adults generally, about half of the ALP in the serum comes from bone¹, although there still is cross-reactivity of up to 20% between the bone liver enzymes.² Osteocalcin in the other large peptide, its
Rheumatoid arthritis is characterized by persistent joint synovial tissue inflammation. Over time, bone erosion, destruction of cartilage, and complete loss of joint integrity can occur. Eventually, multiple organ systems may be affected. Rheumatoid arthritis is the most common inflammatory arthritis, affecting 0.8 percent of the adult population worldwide. Onset usually occurs between 30 and 50 years of age. Incidence in the United States is estimated as 25 per 100,000 persons for men and 54 per 100,000 persons for women. In India several studies reported that a prevalence of RA for total study populations, the prevalence ranged from 0.28% -0.7%.

The incidence of Osteoporosis and fractures is also increased in patients with rheumatoid arthritis. Influence of abnormalities in the bone formation and bone loss is not clear yet. Levels of the bone formation markers have been reported to be normal or elevated or reduced. Therefore in the present study we select 28 Rheumatoid arthritis patients and compared with 42 normal healthy controls.

**Risk factors**
Mainly females, Older aged, silicate exposure, a positive family history and smoking are associated with increased for developing RA. Consumption of coffee more than three cups daily may also contribute. High intake of Vit D, tea consumption and oral contraceptive use are decreased risk of RA.

**MATERIAL AND METHODS**
58 patients suffer from Rheumatoid arthritis (23 males and 35 females) were attained the orthopaedic OPD in the Chandulal Chandrakar Memorial Medical College and Hospital Kachandur, Durg (CG), mean age between 45 -70 and 42 subjects age, sex matched was selected for control group. Controls were mentally, clinically and physically normal and healthy. Study was cleared from Ethical clearance committee of CCM medical college.

### Table 1: Sex wise distribution of Rheumatoid arthritis patients and controls.

<table>
<thead>
<tr>
<th>Groups</th>
<th>No of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Healthy Group</td>
<td>42</td>
</tr>
<tr>
<td>Normal Healthy males</td>
<td>18</td>
</tr>
<tr>
<td>Normal Healthy Females</td>
<td>24</td>
</tr>
<tr>
<td>CVD patients</td>
<td>58</td>
</tr>
<tr>
<td>Male Rheumatoid arthritis patients</td>
<td>23</td>
</tr>
<tr>
<td>Female Rheumatoid arthritis patients</td>
<td>35</td>
</tr>
</tbody>
</table>

**Sample Collection**
Early morning 5 ml fasting blood sample was collected in plain dry test tube. Serum sample was obtained by centrifugation and sample were immediately separated into another plain dry test tube and stored at -20°C. Serum sample was used to estimation of serum alkaline phosphatase (ALP) by pNPP method. Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values p < 0.001 were considered statistically significant.

**OBSERVATIONS AND RESULTS**
Present study was conducted on 42 control subjects and 58 patients who were diagnosed as Rheumatoid arthritis. This study was hospital based case control observational study conducted in CCM Medical College and hospital Kachandur, Durg. Reference range of ALP= 25-147 IU/L Values are expressed in Mean ±SD

- Control Vs Male patients: p < 0.001
- Control Vs Female patients: p < 0.001

Table 3 shows that the level of alkaline phosphatase statically significantly higher in Rheumatoid arthritis patients than normal healthy control group. When Values are compared with normal
control values 15 male patients out of 23 patients ALP level was highly increased found while out of 35 female patients 26 female patients ALP level highly increased found. Increased level of ALP indicates that the disease is more active.

Table 2: Age wise distribution of the control subjects in 45-70 yrs and Rheumatoid arthritis patients were listed below.

<table>
<thead>
<tr>
<th>Age Wise Distribution</th>
<th>Control (n= 42)</th>
<th>Rheumatoid arthritis Patients (n= 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>45-50 Yrs</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>51-55 Yrs</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>56-60 Yrs</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>61-65 Yrs</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>66-70 Yrs</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>24</td>
</tr>
</tbody>
</table>

DISCUSSION

In the present study 58 patients of RA age ranged from 45-70 years (23 male and 35 females) were selected and estimate level of ALP level of ALP (<0.001) was highly significantly increased found in 41 RA patients out of 58 patients than normal control subjects. Main causes of increased level of ALP because of this disease affect the wrist and small joints of the hand and also other parts of the body besides the joints. People with RA may have fatigue, occasional fevers and a general sense of not feeling well. Previous studies reported, the concentrations of serum calcium and Phosphorus are usually reduced and the serum ALP activity was elevated. So our reports also support that the serum ALP was increased in these patients. The relation between serum alkaline phosphatase concentrations and disease activity has not been previously well documented.

Kendall et al. compared 15 patients with rheumatoid arthritis and raised alkaline phosphatase with a similar number of patients with normal alkaline phosphatase and concluded that those with raised alkaline phosphatase concentration had more active disease. It is not clear; however, which clinical parameters of disease activity were determined in their patients. Fernandes et al studied 100 patients and were unable to show a statistical association between serum alkaline phosphatase concentration and severity of arthritis as assessed by articular index, grip strength, and duration of morning stiffness. Unfortunately the numerical data and the statistical methods used are not quoted in their paper. A year later Akesson et al. examined the laboratory data of 182 patients with rheumatoid arthritis. No clinical assessment of disease activity was attempted, but weak correlations were found.
between serum alkaline phosphatase concentration and erythrocyte sedimentation rate and serum orosomucoid values. This present study indicates that serum alkaline phosphatase concentrations correlate with clinical symptoms of disease activity in RA. This may be a reflection of the sensitivity of these clinical parameters as there was significant correlation with plasma viscosity in patients with rheumatoid arthritis. More marked increase in serum alkaline phosphatase concentrations may provide a clue to underlying associated disease, such as hepatic, bone, or even cardiovascular disease.

CONCLUSION
Increased level of ALP indicates that the disease is more active. The increased activity of ALP may be due to its leakage from injured or killed cells. Our study will provide in clinical practice to use the easy and least expensive test, to assess the disease and response to treatment. Very high concentrations of serum alkaline phosphatase may indicate an underlying secondary disease.

REFERENCES

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