Evaluation of Serum osteocalcin in patients with rheumatoid arthritis

Vinod A N*, Nalini Ganesan*, Amarabalan Rajendran*, Rajasekhar G*

1. Introduction

Rheumatoid arthritis (RA) is the most common inflammatory polyarthritis encountered in clinical practice. The prevalence of RA in developing countries in Asia ranges from 0.2 to 1.2%. The prevalence of RA in India is estimated to be about 0.7%. With a population base of 1.2 billion, that translates to a disease load of about 8.4 million [1]. Osteoporosis is a common finding in rheumatoid arthritis. There is almost a two-fold increase in osteoporosis in patients with RA, with a doubling of hip fracture risk [1]. The cellular mechanism responsible for this is unknown, but one possible explanation is an abnormality of osteoblast function or secretion [2]. Osteocalcin, a small 46- to 50-amino-acid non-collagenic peptide is a specific product of the osteoblasts and serum osteocalcin concentrations serve as a marker of bone formation. In several studies [3, 4] it has been shown that mean serum osteocalcin values are reduced in rheumatoid arthritis. suggesting reduced bone formation. Previous studies by Gevers et al [5] and Elenstam et al [6] have also suggested a link between serum osteocalcin levels and disease activity in rheumatoid arthritis. But there aren't many studies in Indian literature to support this link. In the present study we determined to estimate the serum osteocalcin concentration in early RA, late RA and to compare it with healthy individuals suggesting normal rate of bone formation in rheumatoid arthritis.

2. Materials and Methods

This study was carried out in a tertiary care teaching hospital, Sri Ramachandra Medical Centre & Research Institute, Chennai, India. The study protocol was approved by the institutional ethics committee. Fifty one patients with rheumatoid arthritis and twenty four healthy controls were included in the study. Further, patients with rheumatoid arthritis were categorized based on the duration of illness. Patients with RA for two years or lesser duration were classified into early RA and patients of duration more than two years were categorized into late RA. After obtaining informed consent serum samples were collected from all study subjects and osteocalcin levels were estimated by ELISA. Groups were compared in terms of serum osteocalcin concentrations. Statistical analysis was done using SPSS software version 17.1. Results: Serum osteocalcin concentrations were similar in patients with early RA, late RA and control subjects; the duration of RA did not have an influence on osteocalcin concentration. Conclusion: Our study suggests that serum osteocalcin levels do not differ significantly in patients with rheumatoid arthritis compared to healthy individuals suggesting normal rate of bone formation in rheumatoid arthritis.

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estimated by Enzymed-linked immunosorbent assay (ELISA) using Quidel microvue osteocalcin EIA kit (reference range 3.7-10 ng/ml). Rheumatoid factor (RF) and ESR (at 1st hr) levels were also estimated. Groups were compared with respect to serum osteocalcin levels. Comparison of osteocalcin concentrations was also done among RA patients based on age and sex. The data was analysed statistically using SPSS version for Windows statistical program. The results are expressed as mean (SD) values. One way ANOVA was used for the comparison of three groups and student’s t-test was used to compare two groups. Statistical significance was defined as p<0.05. Scatter plot diagram was used to find the correlation of duration of RA with serum osteocalcin concentration.

3. Results

This study included seventy five subjects of which twenty two were early RA, twenty nine were late RA and the remaining twenty four were healthy controls. Early RA group consisted of five males and seventeen females. In the late RA group seven were males and twenty two were females. The control group (healthy subjects) consisted of six males and eighteen females. Characteristics profile of our study sample is shown in table 1. Mean serum osteocalcin concentrations (ng/ml) in groups early RA, late RA and healthy controls were 7.70 ± 1.51, 7.66 ± 1.53 and 7.71 ± 2.28 respectively (Table 2). No statistical significant difference was found among the groups. In RA patients serum osteocalcin concentration did not differ significantly when compared in terms of age and gender (Table 3). In patients with RA, when the duration of RA was plotted against serum osteocalcin concentration in a scattered plot diagram there was no linear correlation between the two indicating that the disease activity does not influence serum osteocalcin levels. (figure 1)

Table 1: Characteristics profile of study subjects

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Early RA (M ± SD)</th>
<th>Late RA (M ± SD)</th>
<th>Normal (M ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects n (%)</td>
<td>22 (29%)</td>
<td>29 (39%)</td>
<td>24 (32%)</td>
</tr>
<tr>
<td>Mean age in years (M ± SD)</td>
<td>38.36 ± 9.50</td>
<td>53.72 ± 8.47</td>
<td>45.58 ± 12.79</td>
</tr>
<tr>
<td>Mean duration of RA in months (M ± SD)</td>
<td>19.4 ± 6.7</td>
<td>84.7 ± 249</td>
<td>-</td>
</tr>
<tr>
<td>Mean serum rheumatoid factor levels (M ± SD)</td>
<td>25.5 ± 8.7</td>
<td>514 ± 549</td>
<td>20.1 ± 18</td>
</tr>
<tr>
<td>Mean ESR(mm) at 1st hr</td>
<td>35.04 ± 9.3</td>
<td>553 ± 15.1</td>
<td>15.3 ± 5.6</td>
</tr>
</tbody>
</table>

Table 2. Comparison of serum osteocalcin concentration (reference range 3.7 - 10 ng/ml) between early RA, Late RA and Healthy controls.

<table>
<thead>
<tr>
<th>Early RA (M ± SD)</th>
<th>Late RA (M ± SD)</th>
<th>Healthy controls (M ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.70 ± 1.51</td>
<td>7.66 ± 1.53</td>
<td>7.71 ± 2.28</td>
<td>0.9°</td>
</tr>
</tbody>
</table>

Table 3: Comparison of serum osteocalcin concentration in RA patients in terms of gender and age.

<table>
<thead>
<tr>
<th>Serum Osteocalcin levels (ng/ml)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>7.20±1.37</td>
</tr>
<tr>
<td>Females</td>
<td>7.83±1.53</td>
</tr>
</tbody>
</table>

Figure 1: Correlation of Duration of RA with serum Osteocalcin concentration.

4. Discussion

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder that may affect many tissues and organs, but principally attacks synovial joints. About 1% of the world’s population is affected by rheumatoid arthritis. Incidence is three times more in women than men. Onset is most frequent between the ages of 40 and 50, but people of any age can be affected. Factors influencing bone mass in RA include patient gender, menopausal status, reduced mobility, disease activity, duration of disease, lack of physical activity, and the concomitant use of corticosteroids[1].

Osteoporosis is a common abnormality in patients with RA. Osteoporosis associated with RA is characterized by relatively preserved bone mass in the axial skeleton and marked loss in the peripheral bone [1]. Compared to the general population patients with rheumatoid arthritis (RA) are two to four times more likely to have osteoporosis. They are also at greater risk of hip and vertebral fractures.

The pathogenesis behind the association of osteoporosis in rheumatoid arthritis is not clearly understood. One possible explanation is an abnormality of osteoblast function or secretion [2]. Serum osteocalcin serves as a marker of osteoblasts function since it is synthesized and secreted by the maturing osteoblasts. Osteocalcin is a vitamin K dependent protein and is the most abundant non-collagenous protein in bone. The presence of osteocalcin in the circulation may provide a specific chemical index of osteoblastic activity [6]. Studies of serum OC concentrations in RA patients have been done in the past. However the results are somewhat discrepant. Gevers G et al [5] in 1986
reported higher serum osteocalcin in RA patients compared to healthy controls. In the same year Ljunghall et al. [6] reported reduced serum osteocalcin concentrations in RA patients. However Pietschmann et al. in 1989 [7] and Franck H et al. [8] in 1992 reported normal concentrations of serum osteocalcin in RA patients. In our study there was no significance difference in serum osteocalcin levels in rheumatoid arthritis patients compared to healthy controls suggesting normal osteoblastic activity in RA patients. Our analysis also suggested that there was no association between duration of RA and serum osteocalcin concentration in patients with rheumatoid arthritis.

5. Conclusion
In conclusion our study shows that patients with rheumatoid arthritis have normal concentrations of serum osteocalcin similar to healthy individuals, suggesting a normal osteoblastic activity (normal rate of bone formation) in rheumatoid arthritis. Future studies with larger sample size may be considered.

6. References