Original Article

Effect of Fibromyalgia Syndrome (FMS) on disease activity (DAS28) Score in patients with Rheumatoid Arthritis (RA)

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Summary:

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease with prevalence of 1% world wide. It is characterized by chronic inflammation of synovial joints, which commonly leads to progressive joints destruction and consequent disability with reduction in quality of life. In some cases it is associated with fibromyalgia syndrome (FMS), is a common systemic disease. It is a very common cause of a multiple regional musculoskeletal (MSK) pain and disability. It commonly associates with medically unexplained symptoms as chronic, widespread pain, asthma, and sleep disorders. When a patient has both RA and FMS, determining the degree of RA activity may be difficult, because these patients typically have higher scores for pain and disability. This study aimed at evaluating whether there were differences in disease activity (DAS28) score between patients with RA and without FMS.

Subjects & Methods: Ninety subjects were included in this study. (30) of them were RA only, (30) were RA/FMS and (30) were healthy control. The patients met the criteria of the American College of Rheumatology (ACR) for the diagnosis of the diseases. The following assessment was made in all patients participating in the study: a clinical history, evaluation of disease activity using the (DAS28) Score and Visual Analogue Scale (VAS), conventional laboratory measurements, and evaluation of the rheumatoid factor.

Results: The study shows that there is no statistical difference in age values. Moreover it reveals that the majority of RA patients are females with female: male ratio of 5:1. It appears that there is no significant difference between the RA groups regarding disease duration. The fatigue state depending on visual analogue scale (VAS) ranged from mild to severe, and most severe state was found in RA-FM group. Rheumatoid factor were more common in RA group, although differences were not significant. BMI (Body Mass Index) was as follows: both RA only group and Control group within overweight state, while RA-FM group is in the obese class I category. The DAS 28 score was significantly higher in RA-FMS than RA only (p < 0.001).

Conclusion: The patients with RA who also have FMS have higher DAS28 scores, and the presence of FM may constitute a marker of a worse prognosis for subjective functional disability.

Keywords: Rheumatoid Arthritis, Disease Activity, Fibromyalgia.

Introduction:

Rheumatoid arthritis (RA) is a systemic autoimmune disease with prevalence of 1% worldwide. It is characterized by chronic inflammation of synovial joints, which commonly leads to progressive joints destruction and consequent disability with reduction in quality of life. RA is a systemic disease, accompanied by progressive joint destruction and deformity. Depending on the severity, there may also be extra-articular manifestations with involvement of the skin, blood vessels, and internal organs. If inadequately treated, RA lead to a significant impairment of the quality of life with increased morbidity and mortality. Early diagnosis and suitable therapy are therefore of decisive importance for the prognosis of RA. The three pillars for the diagnosis of rheumatological disease are the medical history, clinical findings (including imaging techniques) and serological laboratory tests. The American college of Rheumatology (ACR) classification criteria is used to diagnose disease in patients in the appropriate clinical setting, but in early stage of disease is less helpful in establishing the diagnosis because non-clinical measures are often not fulfilled. Therefore, a reliable and specific test early in the disease would be very useful for identifying patients with RA before the occurrence of joint damage and avoid the use of potentially toxic and expensive drugs at these patients. The first ACR criterion through the forth one must be present for at least 6 weeks. These criteria have a sensitivity and specificity of approximately 90%.

Fibromyalgia syndrome (FMS) is a common systemic disease which constitutes a significant public health problem. It is a very common cause of a multiple regional musculoskeletal (MSK) pain and disability. It commonly associates with medically unexplained symptoms in other systems and shows considerable overlap with other rheumatic diseases. Fibromyalgia may occur in isolation (generalized) or may associate with other MSK.
disorders (localized), and is classified as idiopathic (11). It is seen in about 2% of the general population and affects more females than males, with a ratio of 9:1 by ACR criteria (12, 13). It is most commonly diagnosed in individuals between the ages of 20 and 50, though onset can occur in childhood.

Methods:
The study was included on (90) subjects, (30) of them with RA only and (30) patients with RA&FMS and (30) age and sex matched health controls. This study performed during the period from December 2009 to April 2010. These subjects were selected from patients attending the Outpatient clinic in Medical City-Baghdad Teaching Hospital Rheumatology & Rehabilitation Consultation Unit, where the anthropometric tests were performed. The other tests were done in Medical City Teaching Laboratories and the college of Medicine, Department of Physiological Chemistry. Three study groups were investigated which included:

* First group: patients with rheumatoid arthritis only fulfilled the 1987 ACR criteria for RA (RA only group).
* Second group: patients with rheumatoid arthritis and fibromyalgia syndrome according to 1990 ACR criteria for FMS (RA-FMS).
* Third group: Healthy control group who had no history or clinical evidence of RA or any other chronic disease.

Disease activity (DAS28): Active rheumatoid arthritis was defined by the fulfillment of at least three of the following four criteria: Swelling in at least three joints, Tenderness in at least six joints, An ESR ≥ 28 mm/hr, and Morning stiffness of at least 45 min. (14).

DAS28 = 0.56* (SWOLLEN JOINTS) + 0.28* (TENDER JOINTS) + 0.70* LN (ESR, CRP) + 0.014* VAS. (15)

A DAS28 score of higher than 5.1 indicative of higher disease activity, whereas a DAS28 below 3.2 indicate low disease activity. A patient is considered to be in remission if they have a DAS28 lower than 2.6 (14). Statistical methods were used in order to analyze and assess the results. Statistical analyses were done using SPSS. The data were expressed as mean ± standard deviation of mean (SD). The comparison of P-value significance (Sig.) in any test was S: Significant difference (P<0.05), HS: Highly Significant difference (P<0.01), NS: Non Significant difference (P>0.05). The statistical analyses were done by using Pentium-4 computer through the Statistical Package for the Social Sciences (SPSS) program (version-10) and Excel application.

Results:
The study show that the (mean ±SEM) values of age are (44.0 ± 1.49), (48.0 ± 2.36) and (41.7 ± 2.69) for RA-FM, RA ONLY and healthy control groups respectively. Moreover this study reveals that the majority of RA patients are females (50 out of 60)(83.3%) with female: male ratio of 5:1. It appears that there is no significant difference between RA-FM and RA ONLY groups regarding disease duration as (7.97 ± 1.41) and (9.67 ± 1.19) years respectively. The study also reveals that the fatigue state depending on visual analogue scale (VAS) ranged from mild to severe, and most severe state was found in RA-FM group (43.3%) in comparison with (10.0%) in RA ONLY group. Rheumatoid factor were more common in the RA group, although differences were not significant (66.7%) for RA and (66.0%) for RA-FMS. BMI (Body Mass Index) was as follows: both RA ONLY group and Control group within overweight state, while RA-FM group is in the obese class 1 category. In the current study, the DAS 28 score among rheumatoid groups were showed in table (1) and figure (1).

Table (1):- Mean distribution of DAS 28 values among RA patients groups:

<table>
<thead>
<tr>
<th>Studied groups</th>
<th>N</th>
<th>Mean</th>
<th>SD. deviation</th>
<th>ANOVA Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>P-value</td>
<td>Sig.</td>
</tr>
<tr>
<td>RA+ FMS</td>
<td>30</td>
<td>5.76</td>
<td>1.24</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.85 (CRP)</td>
<td>1.43</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.74 (ESR)</td>
<td>1.19</td>
<td></td>
</tr>
<tr>
<td>RA only</td>
<td>30</td>
<td>3.82</td>
<td>1.42</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.74 (CRP)</td>
<td>1.19</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.82 (ESR)</td>
<td>1.42</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>90</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DAS28, disease activity depending on 28 joints: RA only, rheumatoid arthritis alone; RA+FMS, rheumatoid arthritis with fibromyalgia.

Figure (1):- DAS 28 Score among studied groups. RA, rheumatoid arthritis alone; RA-FM, rheumatoid arthritis with fibromyalgia.

In this study there was a high significant difference between the two groups regarding DAS 28 score (DAS 28 CRP was 3.74± 1.19 for RA ONLY group and 5.76± 1.24 for RA-FM group) (p<0.001). In addition, DAS 28 ESR gave the same results. The results of current study showed a significant effect of FMS on disease outcome (activity) in RA patients.
Effect of Fibromyalgia Syndrome (FMS) on disease activity (DAS28) Score in patients with Rheumatoid Arthritis (RA). Abbas M. Ajeeb

Table (2) show a clinical comparison of RA (n= 30) and RA associated with FM (n= 30) patients for the health assessment parameters:

<table>
<thead>
<tr>
<th>Feature</th>
<th>RA</th>
<th>RA-FM</th>
<th>Self-report Assessment</th>
<th>Health professional Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Morning stiffness(min)</td>
<td>3.3</td>
<td>2.1</td>
<td>16.36</td>
<td>9.9</td>
</tr>
<tr>
<td>Tender Joints Swollen Joints</td>
<td>2.9</td>
<td>1.74</td>
<td>3.56</td>
<td>2.6</td>
</tr>
<tr>
<td>ESR</td>
<td>28.2</td>
<td>9.99</td>
<td>24.48</td>
<td>9.09</td>
</tr>
<tr>
<td>CRP</td>
<td>23.37</td>
<td>1.42</td>
<td>5.85</td>
<td>1.43</td>
</tr>
<tr>
<td>DAS ESR</td>
<td>3.74</td>
<td>1.19</td>
<td>5.76</td>
<td>1.24</td>
</tr>
<tr>
<td>DAS CRP VAS</td>
<td>4.2</td>
<td>1.7</td>
<td>5.73</td>
<td>1.74</td>
</tr>
</tbody>
</table>

DAS ESR, disease activity using ESR; DAS CRP, disease activity using CRP; VAS, visual analogue scale.

Discussion:
The difference in DAS 28 score was related to the subjective parameters i.e., tender joints count and global assessment (VAS), which are very dependent on the patient own pain perception, age, and sex (16). The high DAS 28 score in the RA-FM population (5.76:1.24) was in the range of severe activity, whereas that of RA ONLY population (3.8:1.9) remained in the moderate range (17). This observation theoretically leads the physician to increase the burden of treatment in the former population despite the objective measures of disease activity were not so severe (28 swollen count, ESR, CRP), and were comparable to those found in the RA population (18), so the presence of FM in association with RA may have major implications in the interpretation of the DAS 28 score because it is related to higher scores independently to objective evidence of RA activity (19). DAS 28 score is considered essential to evaluate therapeutic response in clinical trials and is useful in classification of disease activity and clinical care (20, 21). Therefore, the possibility that FMS affects the interpretation of this score may have important implications. In routine clinical practice, misclassification of disease activity may lead to an unnecessary change in the therapy of RA patients. It may affect the selection of patients in clinical trials, because a high DAS 28 score is frequently used as one of the inclusion criteria. The interpretation of results may also be affected, because of that FMS are not expected to respond to therapeutics directed toward RA (19). The small difference in objective components and the large disproportion in the subjective components suggest that the coexistence of FMS is the cause of an increase in DAS 28 more than would explained by disease activity. Therefore, when FMS is present it is probable that the DAS 28 score does not accurately reflect the inflammatory activity of RA.

Conclusion:
FMS is related to worse scores on the DAS28 in patients with RA. The presence of FMS may have major implications in the interpretation of the DAS28 score because it is related to higher scores independently of objective evidence of RA activity.

References:
7. Kirox J, and Quilly B. Diagnostic criteria in Rheumatoid Arthritis can we predict which patient will require specific anti-rheumatoid treatment? (Int. Exp. Rheum. 3: 1997; 24-9)

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