EVALUATION OF ANTI-CCP ANTIBODIES AND RHEUMATOID FACTOR FOR THE LABORATORY DIAGNOSIS OF RHEUMATOID ARTHRITIS

NAWFAL Y. AL-DABBAGH, BSC, MSC, PHD*
ZHARA A. HASHIM, BSC, MSC **

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ABSTRACT

Background: 1-Assess the correlation between Anti-cyclic citralliated peptide (anti-CCP2) antibodies concentration with some clinical and laboratory parameters of rheumatoid arthritis (RA): 2-Evaluate the differences in the clinical and serological parameters between anti-CCP2+ve and anti-CCP2-ve patients and Rheumatoid factor (RF+ve and RF-ve) patients. 3-Assess the relationship between smoking history and the detection of anti-CCP2 and RF auto antibodies.

Subject and Methods: This is a case-control study carried out on 55 patients with established RA attending the Rheumatology ward of Ibn-Sina Teaching Hospital in Nineveh Governorate during the period from 1st November 2010 to the 1st June 2011 and 35 apparently healthy individuals as a control. Anti-CCP2 antibodies were measured using enzyme linked immunosorbent assay (ELISA). The RF was tested by latex agglutination and ELISA. C-reactive protein (CRP) was measured by Latex agglutination test. Patients' demographic data, disease activity and duration and erythrocyte sedimentation rate (ESR) were also recorded.

Results: Anti-CCP2 antibodies were found significantly associated with RF, total swollen joints (TSJ) and total tender joints (TTJ) counts (p <0.05) while the correlation with ESR, CRP, disease activity score 28 (DAS28) and disease duration was not significant (p>0.05). In RA patients with smoking history and joints deformity, anti-CCP2 antibodies was more often detected. The same results were obtained for RF seropositivity. It was also found that the differences between RF+ve and RF-ve groups were comparable to those between anti-CCP2+ve and anti-CCP2-ve groups except for ESR and CRP.

Conclusions: The study suggests that the seropositivity of RF is inflammation driven, whereas, the appearance of anti-CCP antibodies might suggests pathophysiological properties and a possible contribution to on-going immune activation.

Keywords: RF, RA anti-CCP2 antibody, DAS28, score, rheumatoid factor, rheumatoid arthritis.

Rheumatoid arthritis (RA) is the most common inflammatory joint disease with prevalence between 0.5 and 1% worldwide¹. The precise etiology of RA is unknown but it has been suggested to be an interaction between genetic and environmental factors². The diagnosis of RA is mainly based on clinical signs and symptoms according to latest recommendations of the American College

* Assistant Professor, Department of Medical Analysis Technique, El-Kitab University College, Kirkuk, Iraq.
** Assistant lecture, Department of Pharmacology, College of Pharmacy, University of Mosul, Mosul, Iraq.
Correspondence author to: Nawfal Y. Al-Dabbagh, nawfal.y.aldabbagh@gmail.com, Mobil +9647707404444

Recent research was conducted in Dept. of Microbiology, College of Medicine, University of Mosul, Mosul, Iraq.
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of Rheumatology (ACR) in 1987\(^3\). Within the seven ACR classification criteria, detection of IgM (RF) in serum is the only recommended laboratory marker. Though IgM-RF is measured in most studies and is the most often ordered autoantibody test in laboratory diagnosis, its specificity for diagnosing RA is limited; at very low levels, IgM-RF is present in sera of most people. High concentrations of IgM-RF are not only detected in RA but also in other conditions with polyclonal stimulation to B-cells like viral and bacterial infections or chronic inflammations other than RA\(^4\). The need for a better laboratory marker with a higher disease-related specificity and sensitivity was always evident. Therefore, a new approach for classification of RA was introduced in 2010 by the ACR and the European League against Rheumatism\(^5\). In the "new" criteria, serology and autoimmune diagnostics carry a major weight, as detection of cyclic citrullinated peptide is appropriate to diagnose the disease in an early state, before joint destructions occur\(^6\). An additional connection between smoking and anti-citrulline auto-antibodies provides further potential insight into mechanisms of disease evolution \(^7\). Cyclic citrullinated peptide (CCP) IgG antibodies have been described as highly specific for RA\(^8\). Rheumatoid factors and anti-CCP antibodies have been shown to be useful diagnostic tools particularly in the early stages of the disease and predictive of disease progression\(^9\). Moreover, an anti-CCP antibody appears to be a good prognostic marker that helps in discriminating between erosive and non-erosive disease\(^10\). The disease activity score 28 (DAS28) is used to assess the disease course and treatment outcome and is based on a count of 28 specified joints for swelling and tenderness, ESR or C-reactive protein (CRP) which are the disease activity markers\(^11\).

MATERIAL AND METHODS

In this case-control study, 55 RA patients recruited from Rheumatology Ward of Ibn-Sina Teaching Hospital in Nineveh Governorate and 35 healthy age and sex matched subjects with no inflammatory, infectious or arthritic conditions were compared over a period extended from 1\(^{st}\) November 2010 to 1\(^{st}\) June 2011. There were 50 females and 5 males in the case group and 32 females and 3 males in the control group. The age of the patients ranged from 20-70 years and that of the controls from 21-67 years. The patients were diagnosed as having RA for at least 1 year. The clinical diagnosis was made by an attending rheumatologist according to the 1987 ACR revised criteria. Anti-CCP antibodies were detected using a commercial IgG anti-CCP enzyme linked immunosorbent assay kit (Aeskulisa, Germany), following the manufacturer’s instructions. Briefly, microliter plates were incubated for 30 minutes at room temperature with serum samples diluted at 1:101 in sample buffer. Prediluted anti-CCP standards and positive and negative controls were added to each plate. After three washes with washing buffer solution, anti-human immunoglobulins conjugated to horseradish peroxidase (conjugate) were incubated and reacted with the antigen-antibody complex of the samples in the micrplates. After three further washes, addition of the TMB-substrate generates an enzymatic colorimetric (blue) reaction,
which was stopped by diluted acid (color change to yellow) and the plates were read at 450 nm (optionally 450/620 nm) with automated device within 30 minutes. Anti-CCP antibodies were considered positive when the absorbance value was higher than the cut-off of the kit (18 U/ml). The rate color formation from the chromogen is a function of the amount of conjugate bound to the antigen-antibody complex and this is proportional to the initial concentration of the respective antibodies in the patient sample. IgM-Rheumatoid factor was detected by ELISA kit (DRG instruments GmbH, Germany). The principle of the test is similar to that of anti-CCP. According to the manufacturer's instructions, IgM-RF level <20 U/ml was considered normal while a level > 20 U/ml was considered elevated. Immuno-agglutination tests were used for the qualitative and semi quantitative determination of RF and C 1-reactive protein (CRP) according to the manufacturer's instruction using Plasmatic Laboratory Products (Dorset, DT6 5BU, United Kingdom). ESR was calculated in mm/1st hour unite. Disease activity score28 (DAS28-ESR) was calculated using online calculator by entering the data of tender joint count, swollen joint count of 28 specified joints and ESR for each patient. DAS28 score of higher than 5.1 is indicative of high disease activity, below 3.2 indicates low disease activity and lower than 2.6 is considered remission. All data were expressed as a mean ±SD using standard statistical methods. The statistical methods used for the analysis of the obtained data include unpaired t-test, z-test of one proportion, Pearson correlation and Chi-square test. The statistical test results were considered significant at p < 0.05.13.

RESULTS
This study involved fifty five (55) RA patients; their mean age ±standard deviation (SD) was 47.7±10.9 years (ranged 20-70 years). Fifty out of 55 (90.9%) were females and 5/55 were males (9.09%). The disease duration of these patients had a mean ± SD of 7.08±6.96 years. Thirteen patients (23.63%) had a positive family history for RA. Ten patients out of 55 (18.18%) had a positive smoking history. Controls included 35 subjects with a mean age and standard deviation of 45.2±9 years (ranged 21- 67 years) and comprised of 3 males (8.5%) and 32 females (91.5%). The results of the DAS28 calculation based on ESR (DAS28-ESR) showed that 53/55 patients had high disease activities with a mean ±SD of 5.92±1.13. The laboratory characteristics obtained in the study showed that the anti-CCP2 antibodies were detected in 31/55 (56.36%) of RA patients and in 1/35 (2.85%) of the controls with a significant difference between the two groups (p=0.004). The concentration mean±SD was 195.6±126.5 U/ml. The IgM-rheumatoid factor antibodies detected by ELISA (RF-ELISA) were found positive in 32/55 (58.18%) RA patients and among 6/35 (17.5%) of the controls with a high significant difference between the two groups (p= 0.009). The concentration mean±SD of RF-ELISA was 310±233.2 U/ml and 26.25±6.8 U/ml for the cases and controls respectively. Rheumatoid factor
antibodies detected by latex agglutination (RF-latex) were found positive in 29/55 (52.72%) patients and in 3/35 (8.5%) of the control. The difference between the patients and control groups was highly significant (p=0.000). The concentration mean±SD of the RF-latex test results was 217.3±195.9 U/ml and 4.57±2.2 U/ml for the patients and controls respectively. C-reactive protein was found ≥ 6 mg/L in 48/55 (87.27%) of the RA patients and in 4/35 (11.4%) of the controls. The difference was also significant between the two groups (p=0.04). The concentration mean±SD was 36.6±35.95 mg/l and 4.37±4.95 mg/l for the patients and controls respectively. ESR was measured for patients only and had a mean±SD of 48.36±25.11 mm/hr.

**The correlation between anti-CCP2 antibodies with other parameters of the disease:** The concentration of anti-CCP2 antibodies tested in the 55 RA patients showed statistically no significant correlation with ESR and CRP (p=0.15, 0.35 respectively). However, a significant correlation was noted between anti-CCP2 antibody concentration and RF-ELISA, RF-latex concentration (p=0.023, 0.021 respectively).

The anti-CCP2 antibodies concentration had no significant correlation with disease duration and DAS28 (p=0.102, 0.16 respectively) although there was a high significant correlation between anti-CCP2 antibodies concentration and the total swollen joints 28 (TSJ) count, total tender joints 28 (TTJ) count (p=0.000, 0.002 respectively).

**Differences in the clinical and serological parameters in the anti-CCP2 seropositive and anti-CCP2 seronegative patients:** The data presented in Table 1, showed significant differences between anti-CCP2 seropositive and anti-CCP2 seronegative groups concerning the age, male gender percentage, smoking history and family history (p=0.000, 0.03, 0.02, 0.03 respectively), however; no significant difference was found in the female gender percentage between the two groups (p=0.45). The laboratory tests including ESR and CRP in anti-CCP2 seropositive and anti-CCP2 seronegative groups showed no significant difference (p=0.240, 0.39 respectively), though; high significant differences were found in RF-latex and RF-ELISA both in positivity and concentration in the two groups of anti-CCP2 status (p=0.01, 0.000 for RF-latex and 0.012, 0.000 for RF-ELISA respectively). Table 1, also showed high significant differences for DAS28, TSJ count and hand joints deformities between the two groups of anti-CCP2 status (p=0.005, 0.003 and 0.04 respectively).

**RF+ve and RF−ve groups vs. anti-CCP+ve and anti-CCP−ve groups:** Significant differences were noticed between positive and negative patients for anti-CCP2 antibodies and RF-ELISA regarding DAS28 and smoking history (p<0.05). However, RF positive patients differ significantly from RF negative patients in regard to CRP concentration and ESR (p=0.008, 0.05 respectively) while no such differences were noted in the two anti-CCP2 status as presented in Table 2. Moreover, this study showed that 10/55 (18.18%) of the patients had positive smoking history and 8 patients out of them (80%) were anti-CCP2 seropositive, with a significant difference between the positive and negative anti-CCP2 groups (p= 0.02).
The concentration mean of anti-CCP2 antibodies was higher in smokers than non-smokers (259.7 U/ml vs. 162.45 U/ml respectively, p=0.01).

For RF, 6 out of 10 smokers were RF positive with a significant difference between positive and negative RF groups (60% vs. 40%; p=0.04), Table 8. The mean RF concentration in smoker was higher than for non-smoker (443.03 U/ml vs. 289.29 U/ml respectively, p=0.03).

**Table 1**: Difference in clinical and serological parameters in anti-CCP2 seropositive versus anti-CCP2 seronegative patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total No.</th>
<th>Anti-CCP2-ve (No.=31)</th>
<th>Anti-CCP2+ve (No.=24)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean±SD)</td>
<td>55</td>
<td>50.22±10.64</td>
<td>44.4±10.50</td>
<td>0.000*</td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>4 (80%)</td>
<td>1 (20%)</td>
<td>0.03**</td>
</tr>
<tr>
<td>Female</td>
<td>50</td>
<td>27 (54%)</td>
<td>23 (46%)</td>
<td>0.45 (NS)</td>
</tr>
<tr>
<td>Positive smoking history (%)</td>
<td>10</td>
<td>8 (80%)</td>
<td>2 (20%)</td>
<td>0.02**</td>
</tr>
<tr>
<td>Positive family history</td>
<td>13</td>
<td>9 (69.2%)</td>
<td>4 (30.76%)</td>
<td>0.03**</td>
</tr>
<tr>
<td>ESR (Mean±SD)</td>
<td>55</td>
<td>53.16±23.82</td>
<td>42.166 ±25.89</td>
<td>0.240* (NS)</td>
</tr>
<tr>
<td>CRP+ve (%)</td>
<td>48</td>
<td>29 (60.4%)</td>
<td>19(39.5%)</td>
<td>0.39** (NS)</td>
</tr>
<tr>
<td>CRP+ve (Mean±SD)</td>
<td>48</td>
<td>44.27±35.36</td>
<td>37.26±37.39</td>
<td>0.501* (NS)</td>
</tr>
<tr>
<td>RF-latex+ve (Mean±SD)</td>
<td>29</td>
<td>25 (86.2%)</td>
<td>4(13.79%)</td>
<td>0.01**</td>
</tr>
<tr>
<td>RF-latex+ve (%)</td>
<td>29</td>
<td>226.56±193.03</td>
<td>160±235.15</td>
<td>0.000*</td>
</tr>
<tr>
<td>RF-ELIS+ve (%)</td>
<td>32</td>
<td>28 (87.5%)</td>
<td>4(12.5%)</td>
<td>0.012**</td>
</tr>
<tr>
<td>RF-ELIS+ve (Mean±SD)</td>
<td>32</td>
<td>324.37±228.4</td>
<td>209.43±278.04</td>
<td>0.000*</td>
</tr>
<tr>
<td>Disease duration (Mean±SD)</td>
<td>55</td>
<td>9.27±7.44</td>
<td>4.25±5.17</td>
<td>0.001*</td>
</tr>
<tr>
<td>DAS28 (Mean±SD)</td>
<td>55</td>
<td>6.35±0.94</td>
<td>5.38±1.15</td>
<td>0.005*</td>
</tr>
<tr>
<td>TSJ count (Mean±SD)</td>
<td>55</td>
<td>13.16±6.68</td>
<td>8.25±4.7</td>
<td>0.003*</td>
</tr>
<tr>
<td>Joint deformities (%)</td>
<td>15</td>
<td>9 (60%)</td>
<td>6 (40%)</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

p- Value ≤ 0.05 was considered significant by unpaired t-test (*) and z-test of one proportion (**), NS=non-significant

**The correlation between DAS28 and other laboratory parameters**

There was a significant correlation between DAS28 and the acute phase reactants (ESR and CRP) with a p-value of 0.000 and 0.03 respectively.

There was also a significant correlation between DAS28 and RF-ELISA and RF-latex (p=0.001, 0.005 respectively), no significant correlation was found betweenDAS28 and Anti-CCP (p=0.16) (Table 3).
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**Table 2: 2 RF+ve and RF-regroups vs. anti-CCP+ve and anti-CCP-ve groups**

<table>
<thead>
<tr>
<th>Parameters (mean ± SD)</th>
<th>IgM-RF +ve</th>
<th>IgM-RF -ve</th>
<th>p-value</th>
<th>Anti-CCP2 +ve</th>
<th>Anti-CCP2 -ve</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>32</td>
<td>23</td>
<td>0.32** (NS)</td>
<td>31</td>
<td>24</td>
<td>0.31** (NS)</td>
</tr>
<tr>
<td>Age (Mean ± SD)</td>
<td>50.84±11.03</td>
<td>43.3±9.2</td>
<td>0.00*</td>
<td>50.22±10.64</td>
<td>44.4±10.50</td>
<td>0.000*</td>
</tr>
<tr>
<td>Disease duration (Mean ± SD)</td>
<td>9.45±7.6</td>
<td>3.78±4.24</td>
<td>0.001*</td>
<td>9.27±7.44</td>
<td>4.25±5.17</td>
<td>0.001*</td>
</tr>
<tr>
<td>ESR (Mean ± SD)</td>
<td>53.75±26.12</td>
<td>40.86±22.1</td>
<td>0.052*</td>
<td>53.16±23.82</td>
<td>42.16±25.89</td>
<td>0.240** (NS)</td>
</tr>
<tr>
<td>CRP+ve (Mean ± SD)</td>
<td>50.48±3$</td>
<td>24±28.3</td>
<td>0.008*</td>
<td>44.27±35.36</td>
<td>37.26±37.39</td>
<td>0.501** (NS)</td>
</tr>
<tr>
<td>DAS28 (Mean ± SD)</td>
<td>6.27±0.95</td>
<td>5.39±1.2</td>
<td>0.007*</td>
<td>6.35±0.94</td>
<td>5.38±1.15</td>
<td>0.005*</td>
</tr>
<tr>
<td>Smoking history (%)</td>
<td>6/10 (60%)</td>
<td>4/10 (40%)</td>
<td>0.94**</td>
<td>8/10 (80%)</td>
<td>2/10 (20%)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

NS=non-significant p-value was considered significant by unpaired t-test (*) and z-test of one proportion(***)

**Table 3: 3 Correlation between DAS28 and other laboratory parameters of RA patients**

<table>
<thead>
<tr>
<th>Parameters (mean ± SD)</th>
<th>Anti-CCP2</th>
<th>RF-ELISA</th>
<th>RF-latex</th>
<th>ESR</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28 (mean ± SD)</td>
<td>5.92±1.13</td>
<td>195.6±126.5</td>
<td>310±233.2</td>
<td>217.3±195.9</td>
<td>48.36±25.11</td>
</tr>
<tr>
<td>*p-value</td>
<td>0.16 (NS)</td>
<td>0.001</td>
<td>0.005</td>
<td>0.000</td>
<td>0.03</td>
</tr>
</tbody>
</table>

NS= non-significant, *p-value < 0.05 was considered significant by Pearson Correlation
DISCUSSION
The frequencies of anti-CCP2 antibodies, RF-ELISA and RF-latex positive results were 56.36%, 58.18% and 52.72% of the patients respectively and their frequencies in the control group were 2.85%, 17.5% and 8.5% respectively with a significant difference between cases and controls. The values of these tests were also higher in the RA patients than in the controls with a significant difference. These results demonstrate the value of anti-CCP and RF antibodies in predicting the presence of RA which is in agreement with previous studies. Although RF occurs in 70-90% of patients with established RA, however; population-based studies demonstrated lower rates of RF positivity. For anti-CCP antibodies, there are some variations in the results among different studies ranging from 33%- 87.2%. These variations in sensitivity could be due to different cut-off value, difference in serum dilution, difference in detection technique among reports or difference in unit of expression, differences in disease duration and other clinical characteristics of the groups being tested.

Our study demonstrated that CRP levels were also significantly higher in patients compared to controls. Similarly, Milovanoic et al observed high values of CRP indicative of active inflammation in RA patients. It has been shown in our study that 7 patients (12.7%) had normal CRP levels despite having active disease states and this is in accordance with the finding that CRP is normal in up to about 40% of patients with RA as reported by others.

The anti-CCP antibodies test had been proved by many studies to be useful in identifying those patients who are likely to have clinically significant disease activity. However, no significant correlation was found in this study between anti-CCP2 antibodies concentration and markers of disease activity (ESR, CRP and DAS28). These results are comparable to those stated by other reports. A possible interpretation of such results is that the study design (case-control) precludes detection of an association of changes in anti-CCP titer and disease parameters. Furthermore, this study did not account accurately for multiple different medications received by the patients. Finally, the study sample size precludes identification of a small association between anti-CCP antibody concentration and RA clinical and serological parameters and subjected to possible selection bias. On the other hand, anti-CCP2 antibodies concentration found, in the current study, to be significantly correlated with TSJ and TTJ counts similar to the findings reported by others.

The present finding that anti-CCP2 antibodies does not correlate with inflammatory markers (ESR and CRP) but with the clinical presentation of the disease (TSJ and TTJ count) indicates that anti-CCP antibodies might have an effect, could be a pathophysiological, that involved in RA development, and the lack of a significant correlation with DAS28-ESR score might be due to the effect of ESR on the DAS28 when calculating it as it was reported, in a study by Makinen et al., that in real-life patients, ESR had the greatest effect on DAS28 followed by TJC and SJC.
This study revealed a significant correlation between anti-CCP and RF by latex and ELISA. These results are compatible with the finding of previous studies\textsuperscript{15,22}. It has been proposed that the presence of anti-CCP antibodies correlates with, but does not completely coincide, the presence of RF\textsuperscript{23}.

In this study, no significant correlation was observed between anti-CCP2 and disease duration, such result is in accordance with the finding of other investigators\textsuperscript{24}. In contrast, other studies\textsuperscript{25} proposed that anti-CCP value elevates in proximity to disease onset. The reasons for these discrepancies are not clear and need further exploration.

It was found that there was no significant difference between anti-CCP2 positive and anti-CCP2 negative patients comparing ESR and CRP. On the other hand, a significant difference was found between the two groups regarding DAS28 and TSJ count as anti-CCP2 seropositive group had greater values of these parameters. These could provide us with further information that anti-CCP seropositive patients might express a different clinical form of RA judged against patients lacking these antibodies. The results of different studies were varied. Two reports showed that anti-CCP seropositive patients had more active disease than anti-CCP seronegative patients\textsuperscript{26, 27}.

Rheumatoid factor positivity and level were significantly different between anti-CCP2 seropositive and anti-CCP2 seronegative groups by the two methods of detection used in the current study. This result is in accordance with many other studies\textsuperscript{15}. In other studies of sera obtained before onset of RA\textsuperscript{25}, anticitrulline antibodies were observed prior to the occurrence of RF suggesting that the increase in RF titer might, in some of these cases, be an event secondary to anticitrulline impunity and immune complex formation involving citrullinated antigens\textsuperscript{28}.

Concerning demographical data; age and disease duration were significantly higher in anti-CCP2 positive than anti-CCP2 negative groups. Ronnelid et al\textsuperscript{27}, found that 3.9% of RA patients changed their anti-CCP status from negative to positive with time. This might suggest that, with advanced age or progression of disease onset, anti-CCP status become more frequently seropositive and this might explain why anti-CCP positive group had higher age comparing with negative one.

The present study showed that 13 out of 55 RA patients had positive family history for RA; nine out of these 13 (69.2%) were anti-CCP2 positive and 4/13 (30.76%) were anti-CCP2 negative which revealed a significant difference between the two groups. This result matches with the fact that anti-CCP antibodies were associated with HLA-DRB1 SE as a genetic risk factor for RA development\textsuperscript{29}.

In general, by comparing the data concerning age, disease duration, ESR, CRP, DAS28 and smoking history obtained in the present study for the positive and negative status between anti-CCP and RF antibodies, the results showed that almost all the differences between anti-CCP2 positive and anti-CCP2 seronegative groups were fairly comparable to those between RF positive and RF negative groups with the exception that ESR and CRP (inflammatory markers) were significantly different between RF positive and RF negative groups but there
was no significant difference between anti-CCP positive and anti-CCP negative groups, again, for ESR and CRP. These results might suggest that the presence of RF is inflammation driven, whereas, the appearance of anti-CCP antibodies suggests patho-physiological properties and a possible contribution to on-going immune activation\(^{20}\).

The frequency of RA patients involved in this study who were smokers or ex-smokers was 18.18\%. The frequency of smokers in anti-CCP2 positive group was found to be significantly higher than in anti-CCP2 negative group (80\% vs. 20\% respectively). This is in accordance with some studies that imply a strong association between smoking and anti-CCP antibodies formation\(^{30}\). In addition, the present study showed that the mean anti-CCP2 antibodies titer was higher for smokers than non-smokers (259.7U/ml vs. 162.45U/ml respectively). However, the presence of high anti-CCP2 titer among members of the current non-smokers group might indicate that other environmental factors contribute to anti-CCP formation\(^{31}\). Regarding RF, a higher frequency of RF-ELISA positive patients was found in the smoker group than non-smoker (60\% vs. 40\% respectively) comparably with the findings of other investigators\(^{32}\). The mean RF level in smokers, like anti-CCP2, was higher than non-smokers (443.025U/ml vs. 289.29U/ml respectively). This is in accordance with the study of Padyukov \(et \, al\)^{33}.

In this study, almost all patients were active with a significant association of DAS28 with inflammatory markers (ESR and CRP). These results correlate with previous findings\(^{15,34}\). However, DAS28 was not found to be correlated significantly with anti-CCP2 antibodies\(^{15}\).

In contrast, Onder \(et \, ar\)^{35} stated that higher DAS28 scores associated with anti-CCP positivity as discussed earlier in this study. DAS28 scores also found to be correlated significantly with RF-latex and RF-ELISA titers. Serdaroglue \(et \, al\)^{15} found a significant correlation between DAS28 and RF. Nevertheless, serum RF measurements have not been useful evaluative tests in RA because changes in titers generally occur slowly and often lag behind other markers of RA activity\(^{36}\).

This study has got its own limitations, the studied sample was relatively small, and the results of this study will be more precise if other city hospitals in Iraq were involved. Studies are required to identify patients at early stage of disease before clinical symptoms become apparent. Furthermore, the effects of therapy on anti-CCP antibodies status and/or concentration are required to determine the possibility of using anti-CCP antibodies as a monitor of therapy.

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پیشنهادات:

1. بیانیات نشریه‌های بیشتری به کمکی که این دو بازیگر با هم کنار هم می‌گردند، نشان دهنده بدنی‌های بیشتری از بیماری‌های سلولاری و مواد بهداشتی است.

2. نقش بیشتری در برنامه‌های بهداشتی می‌تواند نقش مهمی در بهبود وضعیت سلامتی کشور داشته باشد.

3. این بازان می‌توانند به کمک‌های بیشتری در برنامه‌های بهداشتی و بهبود سلامتی کشور کمک کنند.

درک مدل‌ها: فاکتوریال بیشتریکر که می‌تواند نشان دهنده سلامتی و بهداشتی بدنی باشند، می‌تواند در برنامه‌های بهداشتی نقش مهمی داشته باشد.

4. بیانیات نشریه‌های بیشتری به کمکی که این دو بازیگر با هم کنار هم می‌گردند، نشان دهنده بدنی‌های بیشتری از بیماری‌های سلولاری و مواد بهداشتی است.

5. نقش بیشتری در برنامه‌های بهداشتی می‌تواند نقش مهمی در بهبود وضعیت سلامتی کشور داشته باشد.

6. این بازان می‌توانند به کمک‌های بیشتری در برنامه‌های بهداشتی و بهبود سلامتی کشور کمک کنند.

درک مدل‌ها: فاکتوریال بیشتریکر که می‌تواند نشان دهنده سلامتی و بهداشتی بدنی باشند، می‌تواند در برنامه‌های بهداشتی نقش مهمی داشته باشد.
الخلاصة

تقييم علاقة المستضد للببتيد الحلقي السترولينيدي والعامل الرثواني للفحص المختبري لالتهاب المفاصل الرثواني

الخلفية والأهداف

1. تحديد علاقة تركيز الأجسام المضادة للببتيد الحلقي السترولينيدي ببعض الدلائل السريرية والمختبرية لالتهاب المفاصل الرثواني.
2. تقييم الفرق في الدلائل السريرية والمصلية بين مجموعة المرضى الموجبين والسالبين لمستضد الببتيد الحلقي السترولينيدي ومجموعة المرضى الموجبين والسالبين للعامل الرثواني.
3. تحديد علاقة التدخين باكتشاف الأجسام المضادة للببتيد الحلقي السترولينيدي والعامل الرثواني.

طرق البحث:

تصميم الدراسة هو مقارنة الحالات المرضية مع الحالات الضابطة. تم جمع عينات الدم لخمس وخمسين مريضا مصاب بالتهاب المفاصل الرثواني ولخمس وثلاثين شخصا صحيا ظاهرا كعينة ضابط من طابق المفاصل في مستشفى بن سيني التعليمي خلال الفترة من الأول من تيرم من 2010 إلى غاية الأول من حزيران 2011. تم قياس الأجسام المضادة للببتيد الحلقي السترولينيدي والعامل الرثواني باستخدام طريقة مقايضة الممتزح المتعلق بالإنزيم. كما قيس العامل الرثواني والروتين التفاعلي ثاء بطريقة مصيلة ملونة (تلازنالاتكس) ثم تسجيل البيانات الديموغرافية، فترة المرض، التشوهات المفصلية وعدد كريات الدم الحمر للمريض.

النتائج:

لوحظ أن فحص الأجسام المضادة للببتيد الحلقي السترولينيدي مرتبط ارتباطا معзнакомا مع العامل الرثواني. التعدد الكلي للمفاصل المتلازمة والتوتر الكلي للمفاصل الوضيعة (0.05) أمالارتباط مع معدل ترسب كريات الدم الحمر، البروتين التفاعلي ثاء، مقاييس عاطفية المرض 28 وفترة المرض (p<0.05) فلم يكن معينا. في مرضى التهاب المفاصل الروتيني المصابين بتشوهات المفاصل وكذلك المرضى الذين لديهم تاريخ تدخين، كان فحص الأجسام المضادة للببتيد السترولينيدي أكثر وجودا من المرضى بدون تشوهات المفاصل أو تاريخ تدخين. نتائج مماثلة تم الحصول عليها في فحص العامل الرثواني. كما لوحظ أن الفرق بين مجموعتي المرضى الموجبين والسالبين للبروتين التفاعلي ثاء كان متوازنا مع الفرق بين مجموعتي المرضى الموجبين والسالبين لمستضد الببتيد الحلقي السترولينيدي ماعدا الفرق في فحص معدل ترسب كريات الدم الحمر والبروتين التفاعلي ثاء.

الاستنتاجات: أقترح الدراسة أن وجود العامل الرثواني هو نتيجة الالتهاب بينما يظهر مستضد الببتيد الحلقي السترولينيدي يمكن أن يوجي بخصائص مرضية، فضفاضة، وباطئية، والإمكانية في التفعيل المناعي المستمر.