**ANTEKERATIN ANTIBODIES AND ANTI-PERINUCLEAR FACTOR AS DIAGNOSTIC CRITERIA FOR RHEUMATOID ARTHRITIS**

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**KEY WORDS:** ANTIEKERATIN ANTIBODIES, ANTI-PERINUCLEAR FACTOR, DIAGNOSTIC CRITERIA OF RHEUMATOID ARTHRITIS.

**ABSTRACT**

Various auto-antibodies have been described in the serum of rheumatoid arthritis (RA) patients, such as rheumatoid factor (RF), Antiperinuclear factor (APF) and antikeratin antibodies (AKA).

**Objective:** The aim of this study was to evaluate the association of AKA with the activity and severity of RA. Also, to assess their diagnostic value in relation to RF and APF, as well as to determine whether measurements of these antibodies are useful to distinguish early RA from other inflammatory connective tissue disorders.

**Methods:** One hundred and ten serum samples from connective tissue (CT) disorders patients who were diagnosed according to the American College of Rheumatology (ACR) criteria were enrolled in this study. They included 68 RA and 42 different rheumatic disorders. They were tested along with 30 serum samples from apparently healthy subjects. AKA and APF were detected with the indirect immunofluorescence (IIF) technique. RF was estimated with latex fixation test (LFT) and then titrated with Rose Waaler test (RW). Detection of erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) were used as disease activity parameters. Hands and wrists x-ray films were obtained from all RA patients for joint damage evaluation.

**Results:** A positive AKA test was found in 48.5% of RA patients and turned to be highly specific for RA cases (disease specificity 95.8%). RF and APA were more sensitive than AKA
in detection of RA (78% and 58.8% respectively) but less specific (83.3% and 90.2% respectively). RF positivity (>1:128) was restricted to RA but occurred only in 39.6% of sero-positive RA cases. AKA fluorescence intensity grade 2 and 3 occurred only in RA patients and in 57.5% of AKA-positive RA cases. APF titer >1:20 was restricted to RA and occurred in 42.5% of APF-positive RA cases. No significant differences were found between RA positive and negative cases of AKA, APF or RF as regards the age or the disease duration. While significant differences were found when positive and negative cases of AKA and RF were compared as regards the ESR, CRP and radiographic changes. A significant positive correlation was found between the degree of positivity of AKA and RF titers. Moreover, a significant positive correlation was found between the degree of positivity of AKA levels and ESR and CRP levels, and also with the radiographic changes.

**Conclusion:** Although less sensitive than RF, AKA are more specific and allow high percentage of RF negative RA to be diagnosed. Furthermore AKA showed prognostic significance, as positive AKA cases seem to correlate with the activity and the severity of RA and can be considered a predicting factor for radiographic damage in early RA.

**INTRODUCTION**

Rheumatoid arthritis (RA) is a systemic inflammatory disorder that mainly affects diarthrodial joints. It has substantial social effect in terms of cost, disability and lost productivity (Lee & Weinblatt, 2001). RA is the most common inflammatory arthritis affecting about 1 percent of the general population worldwide (Firestein, 2001). The prevalence rate of RA was reported to be three per thousand among Egyptian population with more predominance in females (7 per 1000) than in males (1 per 1000) (EL-Badway et al., 1987).

To date, the diagnosis of RA has been based on the American College of Rheumatology (ACR) criteria (Arnett et al., 1987) where the RF is the only auto-antibody included among the diagnostic criteria. Raised titers of immunoglobulin A RF (IgA RF) are detected in 65-86% of RA patients (Gioud-Paquet et al., 1987 and Mageed et al., 1991). Immunoglobulin M RF (IgM RF) is increased in 70-92% of patients (Gioud-Paquet et al., 1987 and Shmerling & Delbanco, 1991). However, their diagnostic specificity for RA is poor since a positive RF is also found in
many other rheumatic and non-rheumatic diseases and sometimes in healthy subjects (Smolen, 1996).

Tests for circulating auto antibodies are used throughout the world for the diagnosis of RA (Aho et al., 1994). Autoantibodies considered to be early sensitive markers for RA include rheumatoid factor (RF), antibodies to the stratum corneum of rat esophagus called antikeratin antibodies (AKA), and antiperinuclear factor (APF) which reacts with an antigen in the Keratohyaline granules located in the cytoplasm of human buccal mucosa cells (Cordonnier et al., 1996).

AKA are antibodies that can be detected with the indirect immunofluorescence technique on cross-section. Antistratum corneum antibodies were generally called AKA probably because of their labeling pattern and also because Keratins are the major component of this epithelial compartment. Keratin is a family of intercellular fibrous and highly complex insoluble proteins exhibiting pronounced heterogeneity. There is strong evidence that both AKA and APF react with the epitopes of a filamentous protein called profilaggrin (Sebbag et al., 1995). These antibodies are proposed as new markers of diagnosis of RA (Vincent et al., 1999) (Genevay et al., 2002). RF, AKA and APF are often detectable several years before the onset of clinical RA and are therefore considered helpful for the early diagnosis of RA (Weyand et al., 1992).

Some researches have suggested that AKA and APF antibodies can be detected in early RA patients with better specificity than RF. Also, they may be present in RF negative patients suggesting a possible diagnostic utility (Serrel, 2001).

The diagnostic value of AKA and APF was largely confirmed by numerous research groups (Hoet & Venrooij, 1992). Their detection, although mainly restricted to specialized laboratories, is now consensually a valuable tool for the diagnosis of RA (Vincent et al., 1998). Moreover, they appear precocious and can even precede the clinical onset of the disease (Von Essen et al., 1993; Scott, 2000 and Sharma et al., 2000).

Significant associations have been reported in several laboratory markers for disease activity and severity, suggesting that AKA and APF may be useful for predicting the outcome of RA (Vittecoq et al., 2001).

Recently, AKA have also been detected in rheumatoid synovial fluids with higher concentration than in related serum samples, suggesting that they might be locally synthesized and possibly play a part in the pathogenesis of RA synovitis (Kroot et al., 2000).
Regardless of the increase in knowledge about AKA and APE, the exact clinical significance of AKA in RA and their relations with other serological markers have remained uncertain (Vasiliauskiene et al., 2001).

**SUBJECTS AND METHODS**

This case control study was conducted on 110 patients, who were recruited from the Outpatient Clinic of the Rheumatology & Rehabilitation Department of Ain-Shams University Hospitals. Blood samples were obtained from 68 RA patients diagnosed according to the revised American College of Rheumatology (ACR) criteria (Arnett et al., 1987). Forty-two age matched patients with different rheumatic disorders, also diagnosed according to the ACR criteria, participated as disease control group (24 systemic lupus erythematoses (SLE) patients, 4 Sjogren’s syndrome (SS) patients, 10 mixed connective tissue disease (MCTD) patients and 3 scleroderma patients. The RA patients group was also subdivided into 2 subgroups according to the duration of the disease at the time of study. Group 1 (early RA) were 23 with a duration less than 1 year and group 2 (long standing RA) were 45 and the disease duration was more than 1 year. Blood samples were also taken from 30 healthy subjects matching the patient’s group in age and sex.

All patients and controls were subjected to the full history taking and thorough clinical examination.

**Laboratory investigations:**

a) Complete blood picture with coulter (sysmex SF-3000).

b) C-reactive protein with immunodiffusion plates (Dade Behring-Germany)

c) Erythrocyte sedimentation rate (ESR) with the standards Westergren method.

d) Assay of rheumatoid factor (RF): RF (IgM) was determined with latex fixation test (LFT) (Omega-diagn-UK) and Rose-Waaler test (RW) (Amboceptor from Dade Behring Germany). Titers of 1:32 or more were considered positive.

**Special immunological tests:**

**Antikeratin antibody (AKA):**

This was performed with IIF according to the method of Incent et al. (1989). Cryostat sections of the middle third of a rat esophagus were obtained from IMMCO diagnostics (USA). Slides were stored at 2-8° C until used. Serum samples were diluted to 1:10 in phosphate buffered saline (PBS) pH 7.4 and incubated on the slides for 30 minutes at 37° C in a moist
chamber. The slides were rinsed twice for 5 minutes in PBS, and then incubated for 15 minutes with a fluorescein labeled anti-human IgB (Immco diagnostic USA). This was followed by rinsing the slides twice for 5 minutes in PBS, air-dried, mounted with Fluoper medium and studied with a fluorescence microscope (Nikon epifluorescent microscope). The test was considered positive when the rheumatoid arthritis specific IgG anti-stratum corneum (IgG AKA) are highly specific for RA, all the other labeling patterns are not disease specific. Positive AKA case was interpreted as semi-quantitative (grade 1, 2 or 3) according to the fluorescence intensity of the stratum corneum.

Detection of antiperinuclear factor:

Was performed according to the method of Janssen et al. (1988) Fresh unfixed epithelial cells from healthy human oral mucosa obtained by scraping the cheek with a metal tongue depressor was used as substrate. To obtain a cell suspension the spatula was rinsed in phosphate buffer saline (PBS) pH 7.4. The cell suspension was washed with PBS once and with colimycin twice. A cell suspension was maid in PBS and the cells were applied drop wise to a microscope slide. 100-200 cells a hole. After having been air-dried at room temperature the cell preparation was used as a substrate in the indirect immunofluorescence technique (IIF). The slides were analyzed with the Nikon epifluorescent microscope. The test was considered positive when at least 5 cells on a slide were seen showing the typical perinuclear immunofluorescent pattern.

Hands and wrists x-ray films

These were obtained from all RA patients and assessed for joint damage according to Larsen’s score (Larsen et al., 1977). Patients were divided into 2 groups, erosive (Larsen’s score>2) and non-erosive (Larsen’s score<2).

Data analysis:

Data were statistically analyzed using SPSS statistical program (version 8). The diagnostic value of different methods were assessed by computing various diagnostic indices according to classical formulas in which true positive (TP) were patients with a positive test, false positives (FP) were controls with positive test, true negatives (TN) were controls with negative test and false negatives (FN) were patients with negative test.

Sensitivity=TP/ (TP+FN) x 100
Specificity=TN/ (TN+FP) x100
RESULTS

Our results showed that in RA patients group (68 patients); RF was found positive in 52 patients (76.5%) while in the other group of rheumatic disorders (42 patients) RF was positive in 10 patients (23.8%). Among healthy control group we found 2 cases out of 30 with positive RF (6.6%). High titer of RF (>1:64) was present mainly in RA patients. In patient with different rheumatic disorders, the titers did not exceed 1:64 (table 1).

Table (1): Rheumatoid factor titers with RW test in RA patients and different rheumatic disorders compared to the control group

<table>
<thead>
<tr>
<th>Studied groups</th>
<th>RF Titer</th>
<th>Positive RF No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;1:16</td>
<td>1:32</td>
</tr>
<tr>
<td>RA</td>
<td>68</td>
<td>16</td>
</tr>
<tr>
<td>Rheumatic disorders</td>
<td>42</td>
<td>32</td>
</tr>
<tr>
<td>Controls</td>
<td>30</td>
<td>28</td>
</tr>
</tbody>
</table>

RF titer more than 1:16 was considered positive
*p<0.05 significant

As regards AKA and APF, we found that in the RA patients' group (86 patients) AKA was positive in 33 patients (48.5%), while APF was positive in 40 patients (58.5%). In the rheumatic disorders group (42 patients), AKA was positive in 3 patients (7.1%) and APF was positive in 6 patients (14.2%). Among healthy controls, we found only 1 case positive for APF (3.3%). AKA fluorescence intensity grade 2 and 3 occurred only in RA patients (57.5%) of AKA positive cases. APF titer >1:20 was restricted to RA and occurred in 42.5% of APF positive cases (table 2).

Table (2): AKA and APF in RA patients and different rheumatic disorders compared to control group

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>AKA GRADES</th>
<th>Positive AKA No. (%)</th>
<th>APF dilution</th>
<th>Positive APF No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>G1</td>
<td>G2</td>
<td>G3</td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>68</td>
<td>14</td>
<td>12</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Rheumatic disorders</td>
<td>42</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>30</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

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APF was considered positive when five positive cells or more were identified on a slide *p<0.05 significant.

There was no significant difference between RA positive and negative cases of RF, AKA and APF as regards the age or the disease duration. While significant differences were found when positive and negative cases of RF and AKA were compared as regards ESR and CRP (table 3).

Table (3): Positivity of RF, AKA and APF in RA patients according to levels of ESR and CRP.

<table>
<thead>
<tr>
<th>Patients group</th>
<th>RF (mean +SD)</th>
<th>AKA (mean +SD)</th>
<th>APF (mean+SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve p value</td>
<td>+ve p value</td>
<td>+ve p value</td>
</tr>
<tr>
<td>Age</td>
<td>46.7+7.4</td>
<td>46.6+7.4</td>
<td>45.6+11.5</td>
</tr>
<tr>
<td>Duration</td>
<td>7.4+0.2</td>
<td>6.2+9</td>
<td>6.1+1.5</td>
</tr>
<tr>
<td>ESR</td>
<td>60.4+13</td>
<td>58.9+15.3</td>
<td>55.6+11.3</td>
</tr>
<tr>
<td>CRP</td>
<td>25.4+2.8</td>
<td>24.3+3.7</td>
<td>24.3+3.2</td>
</tr>
</tbody>
</table>

p<0.05: Significant  
p>0.05: Non-significant

We divided the RA patients group at the start of our study into early RA patients group (No. =23, <1 year) and long standing RA (No. 45 >1 year). The positivity percentage in the early RA group for RF, AKA and APF were found to be 78.2%, 56.5% and 65.2% respectively. On the other hand, in the long standing RA group, the positivity percentage for RF, AKA and APF were 77.7%, 44.4% and 66.6% respectively. There was no significant statistical difference between early and long standing RA as regards the positivity percentage of RF, AKA and APF (table 4).

Table (4): Percentage of positive cases of RF, AKA and APF in RA patients according to disease duration and radiographic changes.

<table>
<thead>
<tr>
<th>RA No=68</th>
<th>Early RA No=23</th>
<th>Long-standing RA No=45</th>
<th>Non-erosive RA No=28</th>
<th>Erosive RA No=40</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ve RF</td>
<td>52 (76 %)</td>
<td>18 (78.2 %)</td>
<td>35 (77.7 %)</td>
<td>15 (53.8 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>+ve AKA</td>
<td>33 (43 %)</td>
<td>13 (56.3 %)</td>
<td>20 (44.4 %)</td>
<td>10 (38.4 %)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>+ve APF</td>
<td>40 (59 %)</td>
<td>15 (65.2 %)</td>
<td>30 (66.6 %)</td>
<td>6 (23 %)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

p<0.05: Significant  
p>0.05: Non-significant
Plain x-ray films of both hands and wrists were done for every RA patient for joint damage and erosions. We found erosive findings in 40 patients and non-erosive findings in about 28 patients. The positivity percentages in the erosive group were 89.4%, 79% and 47.3% for RF, AKA and APF respectively. While they were 53.8%, 38.4% and 23% for RF, AKA and APF in non-erosive RA cases as regards percentage of positivity of RF, AKA and APF (table 4).

Moreover, a significant correlation was found between AKA grades of positivity and ESR ($r=0.430$) and between AKA grades and level of CRP ($r=0.346$). Similarly, the RF titer and APF with AKA grades were significantly correlated ($r=0.482$) ($r=0.516$) respectively.

A significant positive correlation was found between the degree of positivity of AKA and the erosive radiographic changes ($r=0.415$), while no significant correlation was found between APF positivity and disease activity parameters in RA patients (table 5).

Table (5): Correlation study between AKA, APF and the different studied parameters in RA patients:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AKA</th>
<th>APF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$p$</td>
</tr>
<tr>
<td>RF</td>
<td>0.482</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>AKA</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>APF</td>
<td>0.516</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ESR</td>
<td>0.430</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CRP</td>
<td>0.634</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Radiographic changes</td>
<td>0.415</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

As regards the disease sensitivity of RF, AKA and APF, they were found to be 78%, 48.5% and 58.8% respectively. While the specificity of these parameters was found to be 83.3%, 95.8% and 90.2% respectively (table 6).

Table (6): disease sensitivity, specificity of RF, AKA and APF in RA patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>78%</td>
<td>83.3%</td>
</tr>
<tr>
<td>AKA</td>
<td>48.5%</td>
<td>95.8%</td>
</tr>
<tr>
<td>APF</td>
<td>58.8%</td>
<td>90.2%</td>
</tr>
</tbody>
</table>
DISCUSSION

Rheumatoid arthritis is the most common inflammatory arthritis affecting about 1 percent of the general population worldwide (Firestien, 2001). Recent researches had concentrated on identifying the clinical and laboratory abnormalities present in early RA, with the goal of predicting the long-term outcome of the disease (Van Jaarsveld et al., 1999; Scott, 2000; Sedova et al., 2000; Vittecoq et al., 2000 and Paimela et al., 2001). As radiological articular damage can occur within two years of the first manifestation of RA, there is an urgent need for identifying independent predictive factors present at disease onset (Kim and Weisman, 2000).

In this study, RA patient group showed positivity percentage for the RF, AKA and APF represented as 76.5%, 48.5% and 58.8% respectively. In the other rheumatic disorders group, percentage of positive cases were 23.8%, 7.1% and 14.2% for RF, AKA and APF respectively. While among healthy control group, we found two cases of positive RF (6.6%) and only one case positive to APF (3.3%). Statistical significances were found when RA group was compared to the control group and also when compared to other rheumatic disorder group. The low percentage of both AKA and APF in control group reflect their high specificity.

We found in RA patient group, highest sensitivity for IgM RF (76.5%) than for APF (58.8%) and lowest for AKA (48.5%). On the contrary, specificity was highest for AKA (95.8%), followed by APF (90.2%) and lowest for IgM RF (83.3%).

Our results were in agreement with results obtained by Vincent et al., (1999) who reported positivity percentage of 72% and 43% for RF and AKA respectively in their RA patients. Bas et al. (2002) reported similar results to our results and Vincent et al. (1999) results as they found sensitivity for both RF and AKA in their RA patients were 75% and 46% respectively while their specificity were 74% and 94% respectively. The highest figures of positive APF in RA patients were reported by Janssen and his co-workers (1988). They found that 110 of the 127 sera which were tested gave positive results (86.6%). Berthelot et al. (1995) reported nearly similar results to our results as regards positivity of APF in RA patients. They found that the sensitivity of the test was 72% and specificity was 92%.

In our results, high titer of RF (>1:64) was present mainly in RA patients. In the other rheumatic disorders group, the titer did not exceed 1:64, while titers starting from 1:128 occurred only in 39.6% of seropositive cases AKA fluorescence intensity grade 2 and 3 occurred only in RA patients (57.5%) of AKA positive cases. APF titer>1:20 was restricted to RA patients and occurred in 42.5% of APF positive cases. These results are in
agreement with Santos et al. (1996b) and Slack et al. (1998) who stated that APF and AKA were highly specific for RA patients and APF was the most sensitive test and that high titers of both AKA and APF were found exclusively in RA patients. Vincent et al., (1999) reported that in high titers only a few control samples showed positivity for AKA and APF which permit a higher diagnostic specificity to be reached, but on the cost of the sensitivity for diagnosis of RA.

In an attempt to obtain more sharply contrasted findings regarding the prognostic value of AKA and APF, we compared two groups of RA patients, the first one with erosive radiographic findings and the second group without erosive findings. AKA was positive in 79% in erosive group and 28.4% in non-erosive group, and there was a difference between both groups which indicate that AKA and APF may be used as prognostic indices for articular damage and they can be used together with other inflammatory markers as ESR and CRP which have been established by Scott (2000) and Combe et al. (2001) as important indices for severe articular damage in retrospective and prospective studies. Similar to our results Meyer et al. (1997) and Vasiliauskiene et al. (2001) found non-significant difference between RA positive and negative cases of AKA, APF and RF as regards the age or the disease duration, while significant differences were found when positive and negative cases of AKA and RF were compared as regards ESR, CRP and radiographic changes.

In our study among the non-erosive group 13/28 was sero-negative for RF and belong to early RA group. Interestingly, 6 of them had AKA and/or APF positive results. These results were in agreement with Janssen et al. (1988) who reported the presence of 11 cases of positive APF among 20 sero-negative RA patients (55%) Also, Berthelot et al. (1998) who reported 75% positive APF in sero-negative RA patients we found that AKA specifically was positive in 4 RF negative erosive patients, so we suggested that AKA may be a useful supplementation to RF in predicting erosions. Similar suggestions were obtained by Meyer et al. (1997), Kroot et al. (2000) and Vasiliauskiene et al. (2001). To the contrary, Vittecoq et al. (2000) and Bas et al. (2002) stated that IgM RF was the parameter that associated better with radiological distraction. Combe et al. (2001) stated that, radiologic scores and progression at follow up were closely correlated with the baseline values of ESR, CRP level, IgM and IgA RF positivity and APF positivity.

Although, we did not find any significant difference between early and late RA groups as regards AKA and APF, the presence of AKA and APF was higher in early group than in long standing group. This was explained in previous studies that, as the target of APF and AKA seems to
be the same acidic form of profilaggrin (Sebbag et al., 1995; Vincent et al., 1999 and Nogueira et al., 2001).

Van Jaarsveld et al. (1999); Sedova et al. (2000) and Paimela et al. (2001) claimed that determination of one or the other of these antibodies is sufficient for diagnostic or prognostic purposes in early RA. Vasiliauskiene et al. (2001) reported that, these antibodies have been found in early RA and even before the onset of clinical symptoms.

Despite the correlation between AKA and APF fluorescence intensity was obvious we found RA serum samples with intense fluorescence of APF positivity and undetectable AKA. Vincent et al. (1999) reported similar results, as they found discrepancies between AKA and APF, they hypothesized that it could be explained by differences in the nature of antigens that is highly probable that the human antigen and the rat esophagus antigen do not share all epitopes. Our study revealed no correlation between APF positivity and RF titers or between APF and ESR or CRP. Furthermore no correlation was found between APF and the erosive radiological changes in RA patients. These results were in disagreement with Santos et al. (1996a) and Combe et al. (2001) who reported that APF positivity was associated with erosive radiological changes and joint damage in RA patients. In addition, Vincent et al. (1999) reported that the titers of AKA and APF were found to be significantly correlated with RF titers whatever its detection method. Moreover, Van Jaarsveld et al. (1999) reported that APF negative RA patients had significantly lower radiological changes compared to APF positive patients. Also they stated that both RF and APF positive patients exhibited more radiological damage compared to both RF and APF negative patients and that RF and APF-ve and RF-ve APF+ve RA patients had intermediate radiological changes. Aho (1994) and Van Jaarsveld et al. (1999) reported that APF positivity indicated more severe disease in seronegative RA and the most severe cases among RF positive patients.

In our study there was a significant positive correlation between grades of AKA positivity and levels of ESR and CRP, also between AKA positivity and erosive changes in RA patients. Genevay et al. (2002) reported that the presence of AKA or APF early in the course of RA was associated with the disease activity score. They concluded that antifilaggrin antibodies should be included in the initial investigations of patients with early RA and when positive should alert to a high risk of poor outcome.

We found that the most sensitive test was IgM RF (78%) while the most specific test was AKA (95.8) this result was in accordance with Meyer et al. (1997); Vincent et al. (1999); Vittecoq et al. (2000) and Bas et al. (2002). Saraux et al. (2002) stated that IgM RF and Ig G AKA are the best
laboratory tests for discriminating between patients with and without RA, and that combining these tests slightly improves diagnostic value. Aletaha et al. (2002) reported that although APF and AKA are specific markers for early RA, they were rarely used.

Conclusion:
Antikeratin antibodies showed high disease specificity especially when the antibodies are present in high titer and allow high percentage of RF negative RA patients to be diagnosed. Furthermore, AKA showed prognostic significance as regards the positivity grades of AKA seems to correlate with the activity and severity of the disease. AKA positivity may help in early diagnoses and can be considered as a prognostic factor for radiographic damage in early RA.

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الأجسام المضادة للكيراتين و العامل المضاد للأجسام حول النواة

كامل تشخيصي لمرض الرثياني المفصلي

من أهم الأجسام المضادة التي ذكرت في مرض الرثياني المفصلي العامل المضاد للأجسام حول النواة والأجسام المضادة للكيراتين.

الهدف من هذه الدراسة هو تقدير دور الأجسام المضادة للكيراتين في تحديد مرض الرثياني المفصلي، وتعزيزه عن باقي الأمراض الروماتزمية وخاصة في مراحله الأولى وعلاقة وجوده بنسبة وجودة بصدحة المرض ونشاطه.

تضم مجموعة البحث 105 مريض و37 من الأشخاص كمجموعة ضابطة. وقد قسمت مجموعه المرضى حسب تصنيفهم الكليكيني إلى مرضى الرثياني المفصلي 68 ومرضى بائقي الأمراض الروماتزمية 42 بالإضافة إلى 30 من الأشخاص من نفس العمر والسن الذين كانوا في البحث كمجموعة ضابطة. وقد أجريت للمجتمع فحص كلينيكي شامل ووازي وبالإضافة إلى الفحوصات الروتينية الشاملة تم استخدام معدلات سرعة الترسيب و البروتين التفاعلي سي كمثرات للنشاط المرضي و تم قياس العامل الروماتويدي بطريقة اللاكسيم تم تحديد مستواهات بطريقة الروزور أما بالنسبة للأجسام المضادة للكيراتين والعامل المضاد للأجسام حول النواة فقد تم تعبيينه باستخدام طريقة الفلوريسنت المناخي المثير.

وقد وجد أن نسبة وجود العامل الروماتويدي والأجسام المضادة للكيراتين وعامل المضاد للأجسام حول النواة في مرض الرثياني المفصلي كانت 76.5% و 48.5% و 58.8% على التوالي. و قد وجدت المستويات العالية من هذه الأجسام المضادة مقصورة إلى حد كبير على مرضى الرثياني المفصلي. و قد وجدت فروق إحصائيات ذات دلالة بين المرضى من ذوي النتائج الموجبة والمフトمة من ذوي النتائج السلبية للأجسام المضادة للكيراتين من ناحية أخرى. و قد وجدت أعلى نسبة تخصص بالأجسام المضادة للكيراتين حيث وجدت 95.8% في حين كانت 90.2% و 83.3% لكل من العامل المضاد للأجسام حول النواة والعامل الروماتويدي.

الاستنتاج: و من هذا يمكن استنتاج أن قياس الأجسام المضادة للكيراتين على الرغم من أنه أقل حساسية من قياس العامل الروماتويدي في مرضى الرثياني المفصلي إلا أن درجة تخصصه العالية تتيح اكتشاف المرض في مراحله الأولى خاصة في المرضى سلبي المصل للعامل الروماتويدي. كما أن العلاقة الطرفية الإيجابية بين مستويات و شدة المرض ونشاطه تتيح التنبو بخط سير المرض مما يساعد في اختيار العلاج المناسب منذ البداية لتلافى المضاعفات.