Anti-CCP Antibody Vs Rheumatoid Factor: A Comparison of Diagnostic Characteristics for Rheumatoid Arthritis

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Rheumatoid arthritis is a common systemic inflammatory disease and the diagnosis is primarily based on clinical manifestations. This study was conducted with the aim of comparison between rheumatoid factor (RF) and anti-ccp antibody tests for the diagnosis of Rheumatoid Arthritis. A total of 312 samples comprising 124 (39.7%) from Rheumatoid arthritis patients and 188 (60.3%) from non-Rheumatoid arthritis patients, were collected. Anti-ccp test was found to be better than Rheumatoid factor in sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Likelihood Ratio Positive, Likelihood Ratio Negative, False Positive Rate, False Negative Rate.

Keywords
Anti-ccp, Rheumatoid arthritis, Rheumatoid factor, ELISA

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Introduction

Rheumatoid arthritis is the most common inflammatory polyarthritis and is prevalent in approximately 1% population globally (Klareskog and Catrina, 2009; Aswani et al., 2017). It is an autoimmune disease that occurs more commonly in women than men (Ronald, 2009).

Approximately 20-30% of untreated rheumatoid arthritis patients become permanently disabled (Rindfleisch and Muller, 2005). Thus, early and accurate diagnosis results in better treatment modality and lengthens healthy life. In 1998, Schelleken reported that antibodies, against citrullinated peptide, are highly specific seromarker for the diagnosis as well as prognosis of rheumatoid arthritis, before that rheumatoid factor (RF) was the only serological marker for the diagnosis of rheumatoid arthritis (Schellekens et al., 1998; Hill et al., 2003).

The diagnosis of rheumatoid arthritis depends primarily on the American College of Rheumatology (ACR) criteria.

A patient is considered to be suffering from rheumatoid arthritis if at least four of the seven criteria have been present for at least six weeks; of which the only laboratory test criterion is the presence of serum Rheumatoid Factor (RF) or anti ccp (Banal et al., 2009). Rheumatoid factor is IgM autoantibodies that are directed against Fc portion of IgG antibody, whereas anti ccp antibodies are IgG
antibodies against citrullinated peptides. Anti ccp is not routine laboratory test in resource limited settings due to the less availability of related literature and skill requisite ELISA procedure compared with simple latex agglutination in RF test (Bineeta et al., 2015; Van Pruijn, 2000).

This study was conducted to compare RF with anti ccp antibody detection for the diagnosis of rheumatoid arthritis.

Materials and Methods

A total of 312 serum samples were collected from suspected cases of rheumatoid arthritis. Samples were subjected to RF detection by latex agglutination method and anti ccp antibody detection by Enzyme linked immune sorbent assay (ELISA) (Hotgen biotech, Beijing) as per manufacture instructions with the cut off at 8 IU/ml and 25 Units/ml respectively.

Diagnostic characteristics of both the tests were calculated in respect of sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV), Likelihood Ratio Positive, Likelihood Ratio Negative, False positive rate (FPR) and False negative rate (FNR) by SPSS software 20.0.

Results and Discussion

Out of 312 samples, 64 (20.5%) were from males and 248 (79.5%) were from females with male to female ratio of 1:4 (chart 1).

A total of 124 (39.7%) patients were diagnosed on the basis of American College of Rheumatology (ACR) criterion.

Most of the patients were between the age group of 41-50 years and it was found that rate of positivity increases as the age advances (chart 2). The results of RF and anti ccp antibodies were detected in 82.3 % (96/124) and 83.1 % (99/124) patients respectively. (Table 1 and 2).

The present study was conducted to facilitate the clinicians to confirm the diagnosis of rheumatoid arthritis.

Majority of the patients (83.1%) were female that correlates with the studies conducted by (Sebbeg et al., 1995; Vincent et al., 1989; Nienhuis et al., 1964). In this study, incidence of rheumatoid arthritis was found to be high in age group above 60 years (59.4%) and lower incidence in age group of 11-20 years (20%). The mean age group of the patients was 46.2 years.

Rheumatoid factor was to be positive in 77.4% and anti-ccp antibodies were detected in 79.8% positive cases respectively, similar results (77% and 81%) were reported by (Oommen et al., 2011). Another study by Ayisha et al., reported 76% & 78% sensitivity of RF and anti-ccp test respectively (Ayesha, 2017).

Other studies conducted by Munevver et al., (65%), Sibel et al., (60%), Machold et al., (55%) and Nehir et al., (44.8%) have documented less sensitivity of anti ccp antibodies (Munevver et al., 2008; Sibel et al., 2004; Machold et al., 2007; Nehir et al., 2005).

This could be due to the method of selection of suspected cases. In present study, specificity of RF was found to be less (82.4%) as compared to that of anti-ccp antibody (98.4%). Our study goes parallel with the studies conducted by Ayesha et al., (86%, 98.6%), Sibel et al., (86.4%, 98.6%) and Lee et al., (80.3%, 90%) of RF and anti-ccp antibodies (Ayesha, 2017; Sibel et al., 2004; Lee and Weisman, 2006).
### Table 1: Diagnostic characteristics of RF detection for the diagnosis of RA

<table>
<thead>
<tr>
<th>RF test</th>
<th>ACR criterion</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
<th>False positive rate</th>
<th>False negative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>77.4</td>
<td>82.4</td>
<td>74.4</td>
<td>84.7</td>
<td>4.4</td>
<td>0.27</td>
<td>0.18</td>
<td>0.23</td>
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<tr>
<td></td>
<td>Negative</td>
<td>96</td>
<td>33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>28</td>
<td>155</td>
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</tbody>
</table>

### Table 2: Diagnostic characteristics of anti-CCP antibody detection for the diagnosis of RA

<table>
<thead>
<tr>
<th>Anti-CCP test</th>
<th>ACR criterion</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
<th>False positive rate</th>
<th>False negative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>79.8</td>
<td>98.4</td>
<td>97.1</td>
<td>88.1</td>
<td>50.0</td>
<td>0.2</td>
<td>0.02</td>
<td>0.2</td>
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<tr>
<td></td>
<td>Negative</td>
<td>99</td>
<td>3</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>25</td>
<td>185</td>
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</table>
The present study concludes that detection of anti-ccp antibodies is an important test and may help the clinicians to make early detection and management of Rheumatoid arthritis.

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