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Clinical Utility of Rheumatoid Factor and Anti Ccp Antibodies in the Diagnosis of Rheumatoid Arthritis

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Abstract
Rheumatoid arthritis is an inflammatory joint disease characterised by multiple deformities and associated with considerable morbidity and mortality. The combination of IgM RF and anti ccp antibody increase the ability to detect RA early and to prevent erosive and progressive disease**.** 50 patients with RA and 50 non RA patients were included in the study. Serum were tested for RA and Anti ccp antibody by latex agglutination test and ELISA respectively. RF was positive in 34(68%) of RA and 15(30%) of non RA. Anti ccp antibody was positive in 38(76%) of RA and 1(2%) of non RA. The sensitivity of RF was 68% and specificity of was 73%.The sensitivity and specificity of Anti ccp antibody was 76% and 97% respectively. Anti ccp antibody testing combined with RF has additional value in the diagnosis of RA over RF alone.Anti ccp antibody detection proved to be a powerful diagnostic tool especially in sero negative arthritis.

Keywords: Rheumatoid arthritis, Rheumatoid factor, Anti ccp antibody, ELISA, latex agglutination.

Introduction
Rheumatoid arthritis is an inflammatory joint disease characterised by multiple deformities and associated with considerable morbidity and mortality [1]. The diagnosis of RA is based on ACR criteria, with the only serological marker being RF in the serum [2]. RF is present in a small number of patients with other diseases like chronic hepatitis, connective tissue diseases, infectious diseases and non-rheumatoid arthritis and 15% of healthy individuals [3, 4, 5, 6].

The combination of IgM RF and anti ccp antibody increase the ability to detect RA early and to prevent erosive and progressive disease [7].

1. Materials and Methods
This was a combined, cross sectional, case control and prospective study, done at microbiology diagnostic laboratory, JJM medical college, Davangere, for a period from June 2012 to May 2013. A total of 100 patients were included in the study. 50 were patients with RA, diagnosed by ACR criteria. 50 were proven cases of HIV, hepatitis, Tb, leprosy and OA, 10 in each group. A total of 50 healthy blood donors (HBD) were taken as controls.

After obtaining informed consent 3ml of venous blood was collected aseptically, serum was seperated by centrifugation and stored at -20 c for testing RF and Anti ccp antibody.

RF was tested by latex agglutination test (AGAPPE DIAGNOSTICS). Anti ccp antibody was studied by 3rd generation ELISA method by using GENESIS CPA, Omega diagnostics.

2. Results
The positivity of RF and Anti ccp antibody in the RA and non RA, and HBD are given in table 1, Graph 1.

Table 2, Graph 2 lists the positivity of RF and Anti ccp antibody in the various non RA group.

Table 3, and 4 and Graph 3 and 4 shows the sensitivity and specificity of RF and Anti ccp antibody respectively.

Distribution of positivity of Anti ccp antibody and/or RF in the groups are given in the table 5 and Graph 5.

Distribution of negatives of Anti ccp antibody and/or RF in the groups is given in the table 6.

The use of Anti ccp antibody in seronegative arthritis is given in table 7 and graph 6.

The sensitivity, specificity, PPV and NPV of Anti ccp antibody and RF alone, and their combined testing is shown in table 8.

3. Discussion

RA is associated with only a few specific auto antibodies like APF, AKA and Anti ccp with many nonspecific antibodies like RF [8, 9].Despite the lack of specificity, RF continues to be a serological test for RA, because of its inclusion in the ACR criteria [10].

It is essential to diagnose and treat RA early, as early control of inflammation prevents joint erosions and damage, and if misdiagnosed as RA by RF alone, they are exposed to the adverse effects of anti-rheumatoid drugs. Therefore it is important to include more sensitive and specific tests in the diagnostic panel of RA [11].

On analysis, the sensitivity of RF is 68%, which is in concordance with other studies yielding a sensitivity of 62 and 60% [12, 13].

Specificity of RF in our study was 73%which was low, when compared to other studies [14, 15, 16]. This might be due to the cross sectional nature of this study that included different groups,small sample size and short duration of the study.

Sensitivity of anti CCP in this study is 76% which is comparably similar to other studies yielding a sensitivity 75-85% [17, 18, 19]. Specificity of anti CCP is 97 % which is similar to other studies with specificity of 95.5% and 90 % [20, 18]

Present study showed a higher sensitivity of combined test positivity of RF and Anti ccp antibody in RA.This might be due to the prompt selection ofcases in ous study and the advanced type of kit we used.

Specificity of combined test positivity is 97% which shows testing both RF and Anti ccp would arrive at prompt diagnosis of RA.

Among the non RA groups tested for RF and Anti ccp antibody as shown in table 2,there is increased false positivity of RF than Anti ccp antibody indicating a better specificity of Anti ccp than RF.

As indicated in table 7, 27% of seronegative arthritis were diagnosed by Anti ccp antibody making Anti ccp antibody more sensitive.

Table 7 showing the sensitivity, specificity, PPV and NPV clearly indicates that Anti ccp antibody test alone is more sensitive and specific for RA, and RF is equally sensitive and less specific than Anti ccp antibody test.

Having a positive result of anti ccp antibody and RF is less sensitive and more specific in contrast to the positive result obtained by the indivijual testing of RF/Anti ccp, which is moderately sensitive and equally specific.

On the other hand Anti ccp antibody/RF negative or any one positive is more sensitive and less specific than the combination test of both these factors.

Out of the 50 HBD taken as controls 12 were positive for RF and 2 for Anti ccp. It could be due to the false positivity or ability of anti ccp to detect preclinical RA. These cases could not be followed up.

4. Conclusion

This study clearly concludes that testing Anti ccp positively gives an additive value as a diagnostic tool,and in differenciating or excluding it from other arthritis and non rheumatological conditions.

5. Tables and Images

Table 1: RF and Anti CCP positivity in RA and non RA and HBD

	Anti CCP	RF
RA (n=50)	38(76%)	34(68%)
Non-RA(n=50)	1(2%)	15(30%)
HBD(n=50)	2(4%)	12(24%)

Graph 1

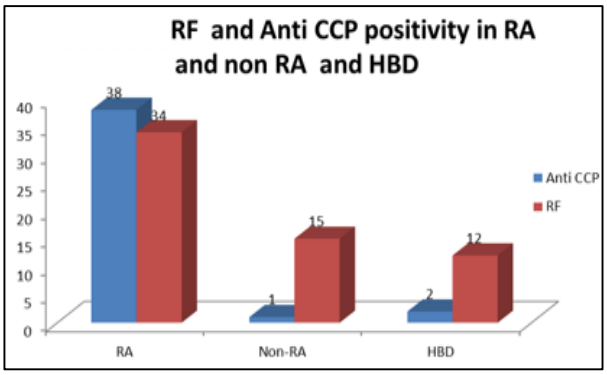


Table 2: RF and Anti CCP positivity in the different Non RA group

Category	RF	Anti CCP
OA (n=10)	6(60%)	1(10%)
TB(n=10)	2(20%)	0
Leprosy(n=10)	0	0
HIV(n=10)	3(30%)	0
Hepatitis(n=10)	4(40%)	0

Graph 2

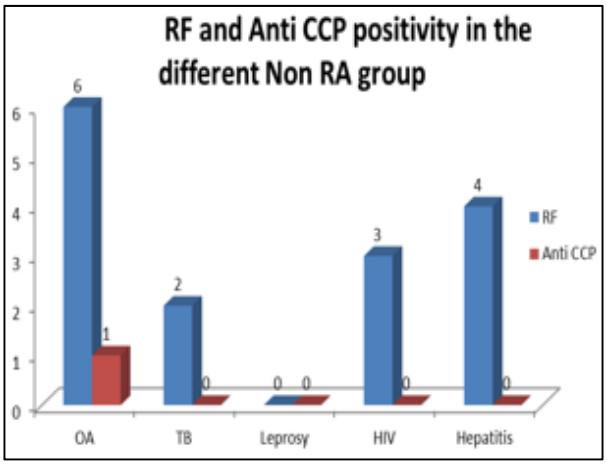


Table 3: Sensitivity and Specificity of RF test in RA

RF	Positive	Negative	Total
RA	34	16	50
Non RA	27	73	100
Total	61	89	150

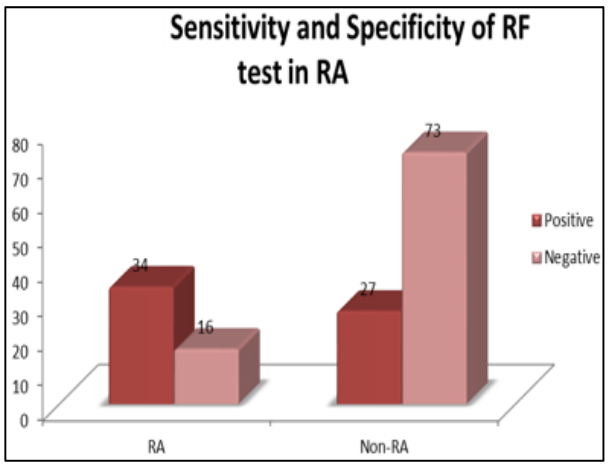
Sensitivity is 68% Specificity is 73%

Table 4: Sensitivity and Specificity of Anti CCP test in RA

Anti CCP	Positive	Negative	Total
RA	38	12	50
Non RA	3	97	100
Total	41	109	150

Sensitivity is 76% Specificity is 97

Graph 3



Graph 4

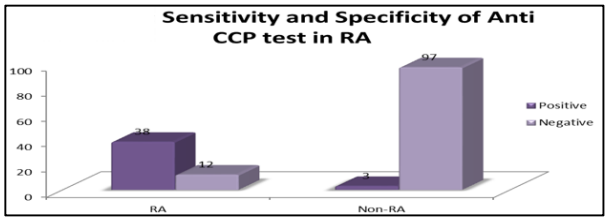


Table 5: Distribution of Positives of Anti CCP and / or RF in the groups.

	RA(n=50)	NonRA(n=50)	HBD(n=50)
Anti CCP (-)	**12(24%)**	**49(98%)**	**48(96%)**
RF (+)	**2(4%)**	**0**	**0**
RF(-)	**10(20%)**	**49(98%)**	**48(96%)**

Table 6: Distribution of Negatives of Anti CCP and / or RF in the groups.

	RA(n=50)	Non RA(n=50)	HBD(n=50)
Anti CCP(+)	**38(76%)**	**1(2%)**	**2(4%)**
RF (+)	**32(64%)**	**1(2%)**	**2(4%)**
RF (-)	**06(12%)**	**0**	**0**

Graph 5

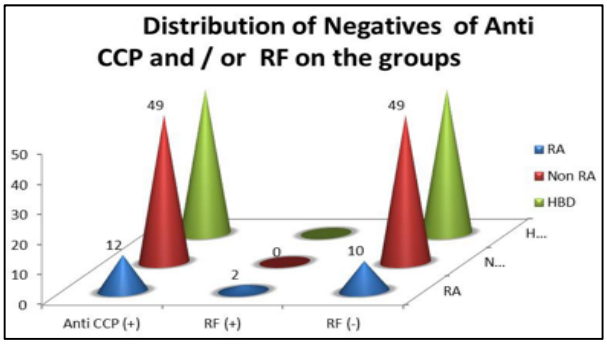


Table 7: Use of Anti CCP in Seronegative arthritis

Anti CCP	Seronegative (RF-ve) (RA – 16)
Positive	**6**
Negative	**12**

Graph 6

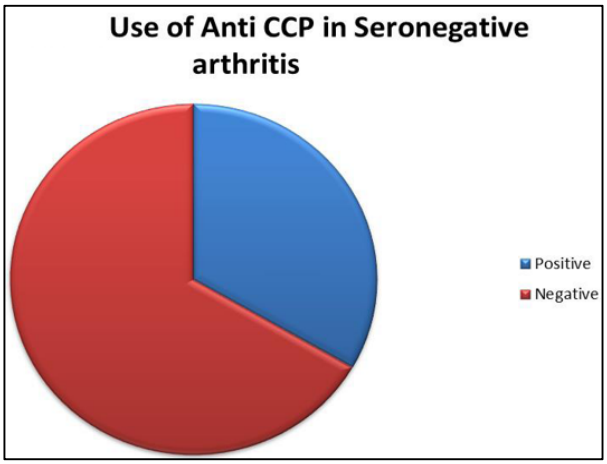


Table 8: Sensitivity, specificity, PPV and NPV of Anti CCP and RF test

Test	Sensitivity	Specificity	PPV test%	NPV test%
Anti CCP	76%	97%	92%	88%
RF	68%	73%	40%	82%
Anti CCP + RF	64%	97%	91%	84%

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