Search For a Biomarker For The Diagnosis And Prognosis of Rheumatoid Arthritis

Prasanth G, Sunil Rao Padmaraj, Vijayakumar T & Riju Mathew

Abstract

Rheumatoid Arthritis (RA) is one of the commonest systemic autoimmune disease. Diagnosis of Rheumatoid Arthritis is based on the detection of Rheumatoid factor (RF) and Anti cyclic citrullinated peptide Antibody (ACCP) .But these markers have limited use in predicting the prognosis of the disease. Hematological and Inflammatory markers are indicators of disease activity .Correlation of the various biomarkers would be beneficial in effective treatment and management of the condition .An attempt is being made to correlate the conventional markers like RF and ACCP with the newer marker Anti Sa Antibody (Anti Sa) and hematological parameters such as Hemoglobin (Hb) , Red cell Distribution Width (RDW) and Erythrocyte Sedimentation Rate (ESR).It was observed that these parameters together serve as better biomarkers for the diagnosis and prognosis of RA.

Index terms

Rheumatoid Arthritis, Anti Sa Antibody, Anti cyclic citrullinated peptide (ACCP), Rheumatoid factor(RF), Chemiluminescence microparticle Immunoassay (CMIA) ,Immunonephelometry,Red cell distribution width (RDW),Erythrocyte sedimentation rate (ESR),haemoglobin (Hb)

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Introduction

Rheumatoid arthritis is one of the commonest autoimmune disorders affecting the joints causing mild inflammation to serious complications. Detection of Rheumatoid factor was considered as the diagnostic tool until the more specific markers like cyclic citrullinated peptide antibodies(ACCP) were discovered [1,2]. ACCP is now considered as one of the very specific marker for RA. But most of these markers has very poor prognostic value and often present in detectable amounts even after appropriate treatment and management [3]. Recently, a new immunological marker Anti Sa was discovered which has very high specificity for RA with relatively low sensitivity when compared to RF & ACCP [4]. There are studies which highlights the prognostic significance of Anti Sa especially in the diagnosis and management of cases of erosive arthritis [5]. Hematological abnormalities especially high ESR and increased levels of inflammatory markers like C Reactive protein (CRP) and fibrinogen is also associated with RA.

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There are studies indicating a positive correlation between RDW ,ESR & CRP in Rheumatoid Arthritis [6,7]. Anemia is also considered to be factor leading to low haemoglobin concentrations which in turn could affect the red cell distribution width [8].As none of these markers individually is found useful in diagnosis and prognosis, the present study was undertaken to evaluate the conventional and new biomarkers in Rheumatoid Arthritis patients.

Materials and Methods

The study was carried out at Educare Institute of Dental Sciences.

Twenty clinically proven cases of RA as per American college of Rheumatology (ACR) criteria form the test group. Twenty age and sex matched subjects selected from the siblings and the staff of the hospital form the control group. None of the patients were suffering from any disease other than RA while the control subjects had no chronic or acute illness, autoimmune disease and was not on any medication. Blood samples were collected from all the subjects after obtaining their informed consent and the following investigations were carried out. Haemoglobin & RDW using Sysmex KX 21 analyser,ESR by Westergrens method RF, by Immunonephelometry on Siemens BN Prospec analyzer, Anti CCP on Abbott Architect Chemiluminescence microparticle Immunoassay analyzer and Anti Sa by Euroimmun ELISA.
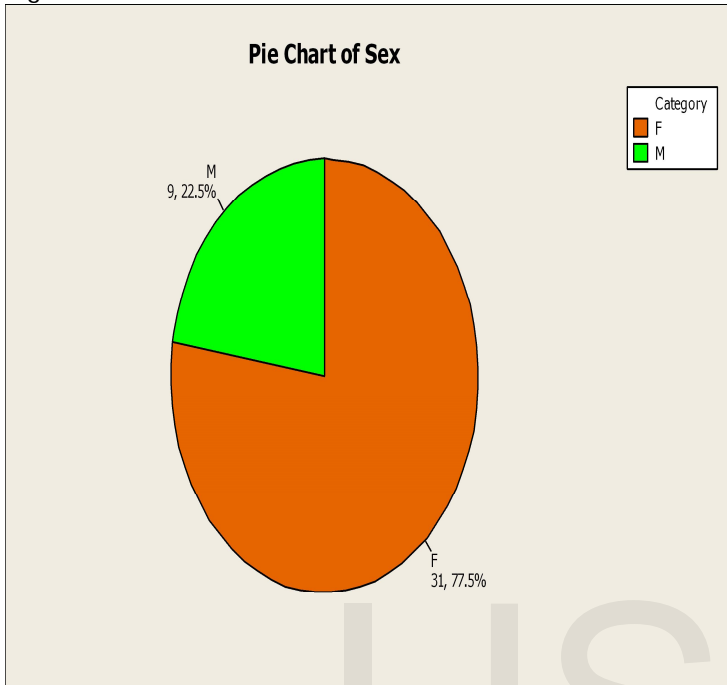
The results were analysed using Minitab & SPSS statistical software.

Results and Discussion

20 patient samples were analyzed for Anti Sa, ACCP and RF during a three month period.20 age and sex matched controls were also included. Female constituted 77.5% of the patients and controls.(Fig 1)

Fig 1

All the patients were in the age group 41-70 yrs . The age wise distribution is explained in Fig 2
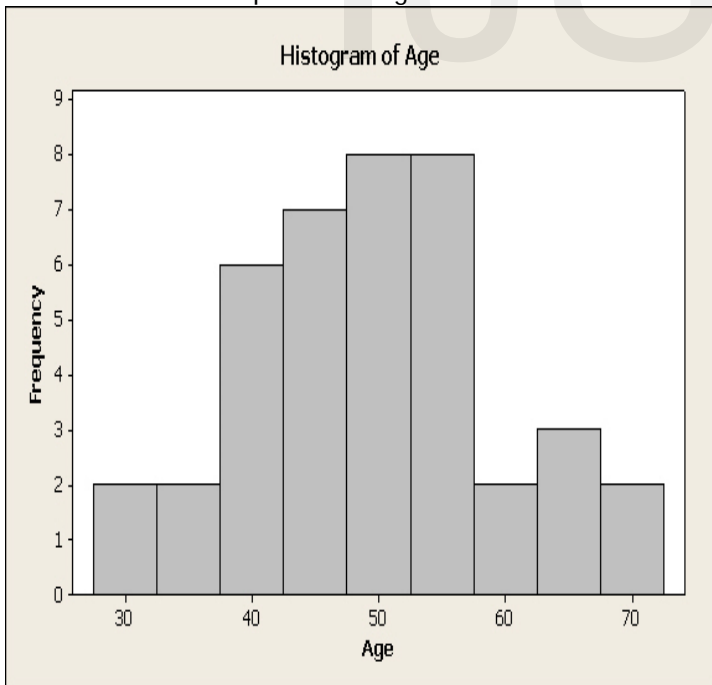
Biochemical and immunological parameters of the patients and that of the controls were statistically analysed. Out of 40 subjects (both patients and controls) (25%) were Anti Sa-positive, (45%) ACCP-positive and (50%) were positive for RF, while in RA patients, Anti Sa, ACCP and RF were positive in (50%), (75%) and (80%)

cases respectively .table 1 elaborates the descriptive statistics of the paramters. There was significant correlation between the Anti-Sa, ACCP, and RF (p<0.01).(table 2) Clinical utility of Anti Sa & Anti cyclic citrullinated Antibody was found to be significant in the earlier studies by *Rodriguez etal & Prasanth etal* .Hematological analysis revealed elevated RDW and ESR and decreased hemoglobin in RA patients compared to normal controls. Hemoglobin levels showed significant negative correlation with all the serological markers. The low hemoglobin levels could be a consequence of anemia in RA patients as suggested by *Lippi etal & Woong etal* RDW was found to be correlating well with the clinical condition of the patient. Optimal management of the patients with RA requires a careful evaluation of the patient for a suitable marker which will help in the prediction of prognosis. Biomarkers are of immense use in various chronic conditions .But unfortunately no biomarker(s) has been proposed adequately to assess the disease activity in RA. The conventional markers like RF and CRP were significantly elevated and showed good correlation with the ACCP. The new serological marker Anti Sa had very high specificity with comparatively low sensitivity. RDW which is reported as a promising marker for renal involvement may also be useful when used in conjunction with the conventional and new serological markers.

Table 1

Descriptive Statistics

	Mean	Std. Deviation	N
ACCP	49.063	74.4504	40
ANTI SA	23.338	39.1094	40
RA	114.7563	239.07128	40
RDW	13.260	1.4872	40
ESR	30.13	32.740	40
Hb	12.618	1.0436	40

.Table 2

Correlations

		ACCP	ANTI SA	RA	RDW	ESR	Hb
ACCP	Pearson Correlation	1	.595**	.632**	.647**	.663**	-.541**
	Sig. (2-tailed)		.000	.000	.000	.000	.000
	N	40	40	40	40	40	40
ANTI SA	Pearson Correlation	.595**	1	.548**	.318*	.663**	-.353*
	Sig. (2-tailed)	.000		.000	.045	.000	.025
	N	40	40	40	40	40	40
RA	Pearson Correlation	.632**	.548**	1	.285	.416**	-.409**
	Sig. (2-tailed)	.000	.000		.075	.008	.009
	N	40	40	40	40	40	40
RDW	Pearson Correlation	.647**	.318*	.285	1	.546**	-.291
	Sig. (2-tailed)	.000	.045	.075		.000	.069
	N	40	40	40	40	40	40
ESR	Pearson Correlation	.663**	.663**	.416**	.546**	1	-.436**
	Sig. (2-tailed)	.000	.000	.008	.000		.005
	N	40	40	40	40	40	40
Hb	Pearson Correlation	-.541**	-.353*	-.409**	-.291	-.436**	1
	Sig. (2-tailed)	.000	.025	.009	.069	.005	
	N	40	40	40	40	40	40

**. Correlation is significant at the 0.01 level (2-tailed).

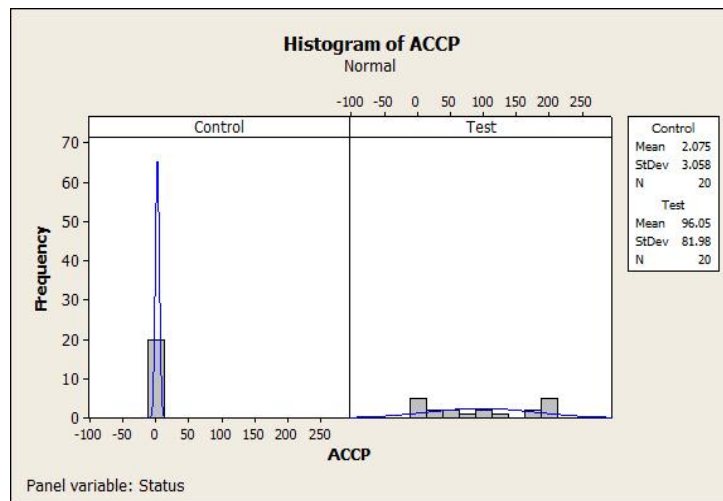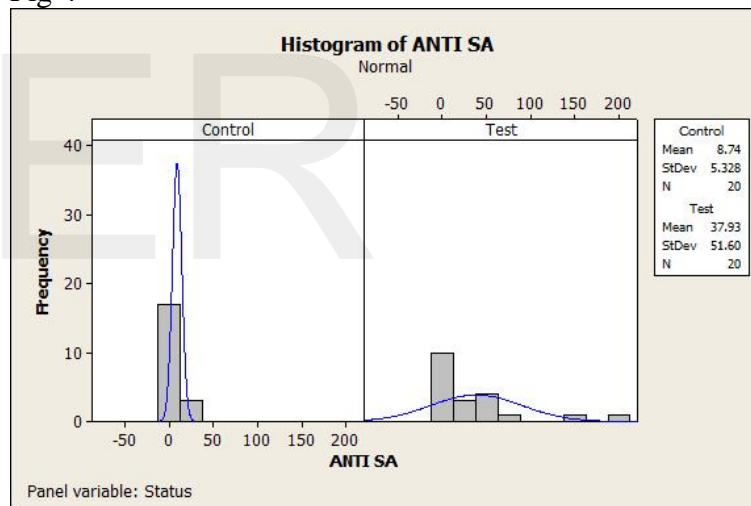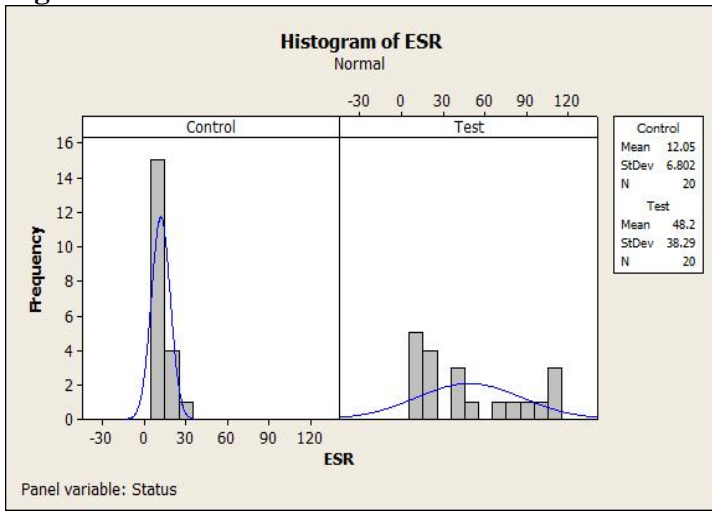*. Correlation is significant at the 0.05 level (2-tailed).

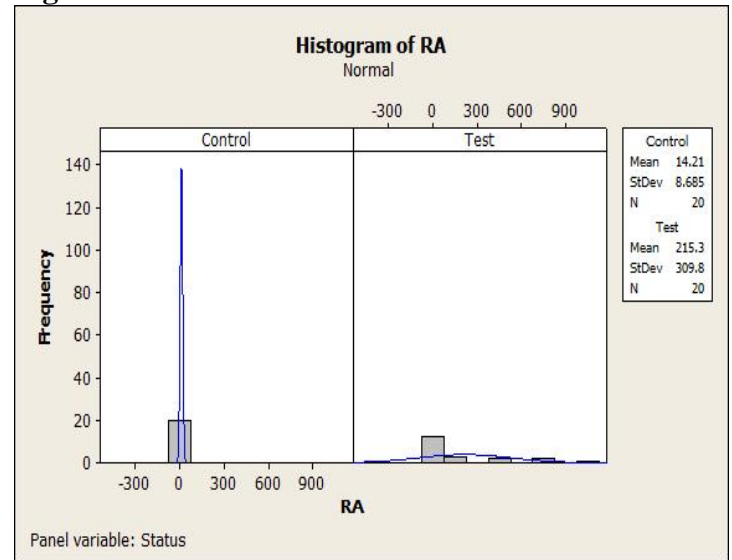Fig 3

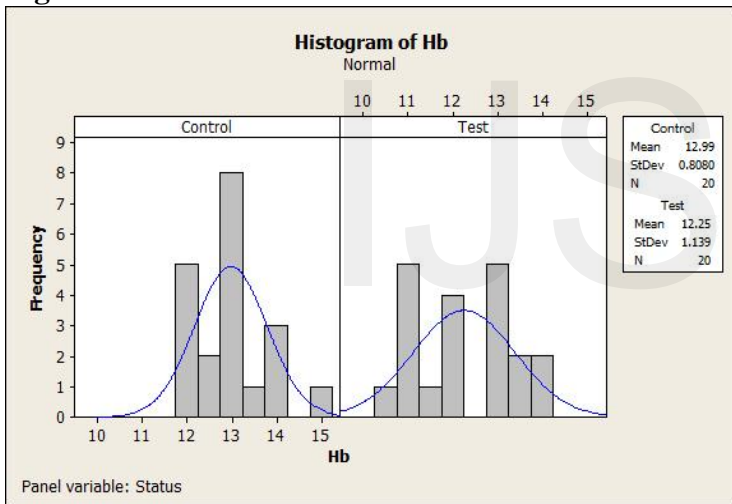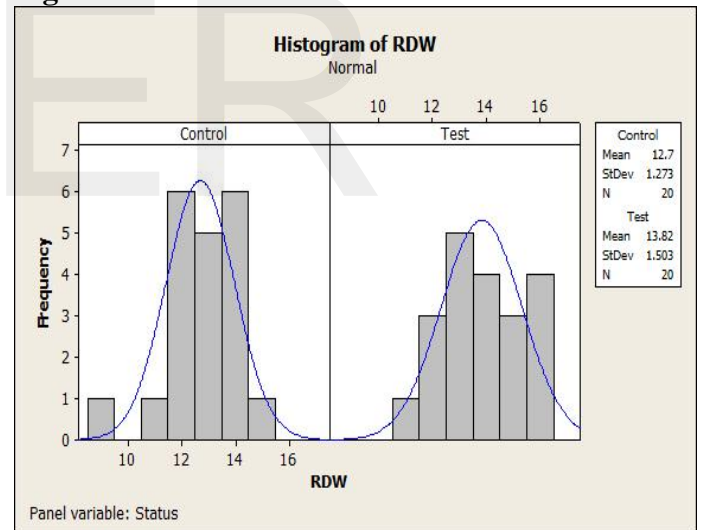

Fig 4

Fig 5

Fig 7

Fig 6

Fig 8

Conclusion

The serological markers Anti Sa Antibody,Anti cyclic citrullinated peptide antibody & Rheumatoid factor in combination serves as good serological markers for Rheumatoid Arthritis. The hematological markers RDW , hemoglobin and ESR reflects the pathological outcomes of Rheumatoid Arthritis. The hematological abnormalities like anemia might be a factor involved in these variations .Nevertheless the hematological parameters in conjunction with the serological markers aids in the diagnosis of Rheumatoid Arthritis

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