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PREDICTIVE MARKERS FOR THE DIAGNOSIS AND PROGNOSIS OF RHEUMATOID ARTHRITIS

Immunology

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ABSTRACT

Rheumatoid Arthritis (RA) is one of the most commonplace systemic autoimmune conditions. Diagnosis of Rheumatoid Arthritis is based on the detection of Rheumatoid factor (RF) .But this parameter had a high specificity for Rheumatoid Arthritis with comparatively low sensitivity and limited use in predicting the prognosis of the disease. Hematological, antioxidant and Inflammatory markers are indicators of disease activity. Interdependence of the various markers would be propitious in effective treatment and management of the condition.Consolidation of novel and conventional markers could be supportive in predicting and helpful in early diagnosis particularly due to the disparity in the clinical presentation and discrepancy in the dispersion of the markers in different patients.

KEYWORDS

Rheumatoid Arthritis, Anti DS DNA, Anti cyclic citrullinated peptide,Vitamin C, Erythrocyte sedimentation rate,haemoglobin

INTRODUCTION

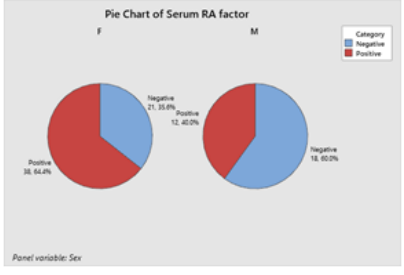
Rheumatoid Arthritis is a chronic inflammatory systemic autoimmune disease with varying degree of morbidity and mortality. The available biomarkers for the diagnosis and prognosis of these diseases are not reliable as many of them are not useful as prognostic indicators. Even though serological markers are available for the diagnosis of RA, no specific biomarkers are available for predicting the outcome of the disease. Hence the present was undertaken to investigate the various Immunological, biochemical, antioxidant and haematological abnormalities in RA patients.

Rheumatoid arthritis is the commonest cause of chronic inflammatory arthritis all over the world including India. The overall prevalence of the disease is around 1% in the general population. Although RA is considered as a condition of the joint, it is important to recognize that it can exhibit a variety of extra-articular manifestation which clearly indicates that this illness has features of a systemic disease and is capable of involving a variety of the main organ systems. The severity varies from mild inflammation in the joints to serious complications. Besides the conventional marker, many serological markers belonging to the citrullinated peptide antibodies are associated with the disease.
Several investigators found an increased risk for the development oflymphoproliferative disorders and lung cancer, but a decreased risk for the development of colorectal malignancies in RA. Long-term inflammatory activity in RA seems to have been associated with increased tumor risk with an odds ratio of 25.8 compared to moderate disease activity. In recent cohort studies, the risk of lymphoma in RA patients was found to be 1.4 to 3.9 times higher than in the general population.

Analysis of various biochemical, immunological and genetic markers helps to identify the deleterious effect caused due to oxidative damage and vulnerability to neoplastic changes. Oxidative stress is increased in autoimmune diseases, and it contributes to immune system dysregulation, abnormal activation, and processing of celldeath signals, autoantibody production, and fatal comorbidities.

Mitochondrial dysfunction in T cells promotes the release of highly diffusible inflammatory lipid hydroperoxides, which spread oxidative stress to other intracellular organelles and through the bloodstream. Oxidative modification of self-antigens triggers autoimmunity and the degree of such modification of serum proteins shows striking correlation with disease activity and organ damage in RA

Group Statistics							
Parameters	Serum RA factor	N	Mean	Std. Deviation	Std. Error Mean	T value	P Value
Serum Anti-CCP (u/ml)	Negative	39	13.41	1.996	.320	-11.8	<0.01**
	Positive	50	366.68	187.366	26.498		
Serum Anti DS DNA	Negative	39	63.67	29.762	4.766	-7.4	<0.01**
	Positive	50	369.94	256.583	36.286		
Hb (gm%)	Negative	39	7.108	4.6250	.7406	-6.5	<0.01**
	Positive	50	11.600	1.4428	.2040		
CRP (mg/L)	Negative	39	7.108	4.6250	.7406	-3.8	<0.01**
	Positive	50	21.220	22.4702	3.1778		
Comp C3	Negative	39	120.33	22.227	3.559	8.3	<0.01**
	Positive	50	72.68	30.160	4.265		
Comp C4	Negative	39	32.05	9.974	1.597	8.5	<0.01**
	Positive	50	15.58	8.219	1.162		
Vitamin C	Negative	39	1.46795	.381894	.061152	14.8	<0.01**
	Positive	50	.67100	.000000	.000000		
ESR	Negative	39	12.08	2.044	.327	-24.3	<0.01**
	Positive	50	36.26	5.934	.839		



The available biomarkers for the diagnosis and prognosis of autoimmune diseases are not reliable as many of them are not useful as prognostic markers. Hence, this study analyses the various pathological markers of RA along with markers for oxidative stress and DNA damage for possible associations in the management of these conditions in patient groups undergoing various treatment modalities.

MATERIALS AND METHODS

Clinically established RA cases with RA factor and Anti-CCP positive forms the test population. The patients did not have any chronic or acute infections or cancer. Both male and female subjects fulfilling the above criteria were included. Normal individuals who are negative for ANA, Anti ds-DNA, RA and Anti-CCP without any infectious or systemic diseases or autoimmune disease and not on any therapy, preferably the siblings of the patients, were included as control.This study was approved by the institutional ethics committee.

Ten mL of venous blood was collected after getting the informed consent. Five ml was collected in vaccutainer with clot activator, serum separated after clot formation and all the serological

investigations were carried out in the serum samples. Out of the remaining 5 ml of blood, 3 ml was collected aseptically in heparinized vaccutainer for genetic studies and 2 ml was collected in vaccutainer containing K3 EDTA for hematological studies and estimation of fibrinogen.

RESULTS AND DISCUSSION

Blood samples from RA patients were tested for serological markers (RF, Anti-CCP & Anti-Ds), hematological markers (Hb& ESR), inflammatory marker (CRP), and antioxidant (Vitamin C). The disease activity score for the patients were provided by the physician. Anti- Ds DNA had high specificity for RA with comparatively low sensitivity. Combination of Anti- Ds DNA and Anti -CCP may improve the sensitivity and could be useful as diagnostic markers for Rheumatoid Arthritis. CRP levels were markedly decreased in RA patients undergoing treatment with biologics indicating decreased disease activity. ESR levels correlated positively with CRP in untreated RA patients possibly due to increased disease activity in these patients. Antioxidant levels may be used as a tool for predicting genetic damage in RA and SLE patients and antioxidant supplementation might be useful to reduce oxidative stress.

CONCLUSION

RA is an autoimmune condition requiring several biomarkers for proper patient management. Some of these markers help in diagnosis while others measure the disease activity and treatment outcome. Combination of novel and conventional biomarkers might be helpful in prediction and early diagnosis especially due to the diversity in the clinical presentation and inconsistency in the distribution of the biomarkers in different patients.

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