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RESEARCH ARTICLE

BIOMARKERS FOR DIAGNOSIS AND DISEASE ACTIVITY ASSESSMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS PRESENTING WITH ARTHRITIS

Prasanth.G*, Sunil RaoPadmaraj*, Riju Mathew*, Vijayakumar.T**

*Medical Research Centre, Yenepoya University Mangalore, **MaheInstititute of Dental Scienes

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***Corresponding Author**

Prasanth.G

Abstract

Systemic lupus erythematosus is one of the autoimmune diseases with complex etiology. Arthritis is one of the commonest manifestations of lupus. There are several serological markers available for the differential diagnosis of SLE. This study compared the diagnostic markers Anti nuclear antibody and Anti ds DNA antibody in untreated SLE patients with Erythrocyte sedimentation rate (ESR) and Complement protein C3 & C4 levels to identify and analyze the relationship and utility of using the different markers in conjunction for the diagnosis of lupus arthritis.

INTRODUCTION

SLE is a complex autoimmune condition characterized by marked breakdown in immunological tolerance[1,2,3]. SLE has a wide range of organ involvement with varying degree of severity. One of the features of SLE is the involvement of autoantibodies which form immune complexes and resultant complement activation is considered as the main cause for the deleterious consequences in SLE patients[4].One of the commonest manifestations of SLE is Arthritis and needs to be differentiated from Rheumatoid arthritis by means of diagnostic tests[5,6].As per the American college of Rheumatology (ACR) criteria, Anti nuclear antibody(ANA), Anti Ds DNA antibody and Anti Sm Antibody can be used as serological markers and detection of complement levels would predict the disease activity[7] .Rheumatoid factor which is a serological marker for Rheumatoid arthritis is also occasionally detected in Sle patients .The non specificity of such markers would often lead to misdiagnosis or delayed diagnosis[8].It is often observed that an increased disease activity during acute phase of SLE would lower the serum complement levels .The resultant immune complex deposition at various organs and the lytic activity of the complement proteins adds to the pathologic manifestations of SLE[9,10]. Hemoglobin level& Red cell distribution width (RDW) are useful hematological parameters in various autoimmune conditions[11]. An elevated ESR is usually associated with infectious diseases like tuberculosis or autoimmune conditions like Rheumatoid Arthritis or SLE. It is essential to analyze various diagnostic markers during the acute condition of a disease to identify the relationship between the markers and to assess the utility of the markers in diagnosis. This study considered lupus patients with Arthritis. Correlation between the serological markers, complement levels and hematological parameters were analyzed.

Materials & methods

The study was conducted at Educare Institute of dental Sciences. Fifteen subjects satisfying the ACR criteria were selected for the study. Age and sex matched normal individuals were included as controls.Blood samples were collected after informed consent .The samples were tested for Antinuclear Antibody (Indirect immunofluorescence Euroimmun Germany), Anti ds DNA NcX ELISA(Euroimmun Germany), C3 & C4 complement levels and CRP by Immuno-nephelometry(SiemensBNProspec), Hemoglobin(Sysmex Kx21Autoanalyser).The results were analyzed using SPSS 17 and Minitab 16. P value less than or equal to 0.05 is considered as significant.

Results& Discussion

Thirty six Rheumatoid factor negative subjects with suspected SLE arthritis were tested for the serological, Immunological and hematological parameters.Female subjects constituted -63.6% of the total(fig 1).The descriptive statistics are detailed in Table 1. 45.5%of the total had positive ANA results (fig2) whereas dsDNA Antibody was positive for 37.5% of the total subjects. Twentyeightpercent of the total had low Hb level, 37.5% had decreased complement c3 &28% had low c4 levels. Forty six percent of the total subjects had elevated RDW. Among the patient group all were positive for ANA, 80% for ds DNA & 60% had low Hb levels. The distribution of dsDNA, CRP, RDW and Hb in test and control group is shown in fig 3 &4.CRP levels were elevated in 93% of pateints. Low c3 levels were found in 80% and low C4 levels in 60% of the patients. RDW was elevated in 86 % of the patient group.ANA & Anti ds DNA levels showed negative correlation with complement levels whereas CRP & RDW showed positive correlation($p<0.005$)Table 2).

Figure 1. Sex distribution of the study subjects

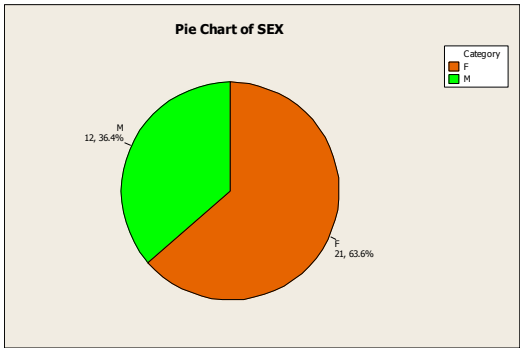
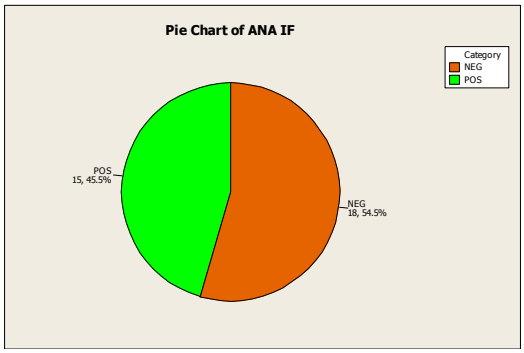


Figure 2. ANA positivity of the study population

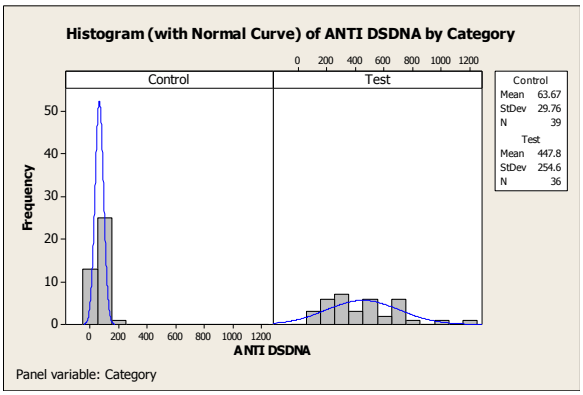


Tabel 1. Desriptive statistics and t test of the study population

Variable	Control (N=39)	Test (N=36)	t Test P value
Age	43.08 ± 11.64	39.47 ± 10.71	0.166 (NS)
Anti DsDNA	63.67 ± 29.76	447.8 ± 254.6	<0.001 (Sig)
C reactive Protein	7.108 ± 4.625	26.89 ± 24.13	<0.001 (Sig)
Hemoglobin	13.864 ± 1.269	11.444 ± 1.443	<0.001 (Sig)
RDW	13.279 ± 1.444	16.719 ± 1.766	<0.001 (Sig)
C3	120.33 ± 22.23	59.39 ± 17.2	<0.001 (Sig)
C4	32.05 ± 9.97	12.972 ± 5.526	<0.001 (Sig)

RDW: Red Cell Distribution Width C3: Compliment C3 . C4:Complement C4 ,
No significant difference in age, but all parameters are statistically highly significant against test and control means.

Figure 3. Anti dsDNA of test and control population



The CRP levels were found to be higher in patients indicating marked inflammatory activity (Figure 4.). *Li etal*had reported reduced CRP levels in Systemic lupus patients compared to Rheumatoid Arthritis subjects[12] while Independent studies by *Eudy etal*[13]*&Pradhanetal*[14]found higher CRP levels useful in detecting active disease and flare.

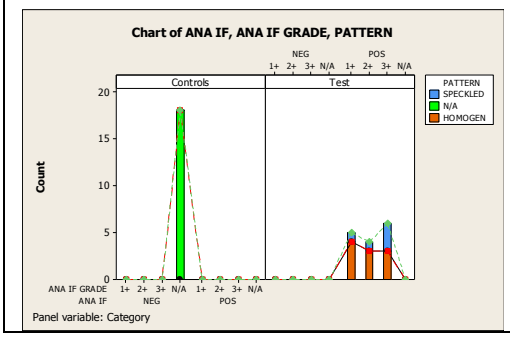
Table 2. Correlation Table of the study parameters

Parameter		ANTI DSDNA
CRP	r	0.499
	p	0.001
HB	r	-0.535
	p	0.001
RDW	r	0.690
	p	0.001
C3	r	-0.721
	p	0.001
C4	r	-0.714
	p	0.001

r: Correlation coefficient, P: Significance

The patterns of ANA observed were mostly homogenous pattern(66%) & speckled pattern(34%).The Immunoflourescence pattern was graded (Figure 5.).The correlation between the various parameters is explained in Table 2.

Figure 4. ANA IF pattern and grade



The studies by *Li etal* highlighted the utility of complement levels in assessing the disease activity. This study also underlines the fact that a positive autoantibody titre with lowered complement levels indicates active disease. High ds DNA Antibody could also be a predictive marker for the development of lupus nephritis and other complications. Earlier studies have shown that during the early stages of the diseases there may not be a considerable difference in C3, C4 and CRP levels in SLE & Rheumatoid Arthritis patients. A low hemoglobin level and a high RDW is often indicative of anemia in auto immune patients and needs further investigation .Chronic blood loss may also contribute to this condition.SLE causes immune complex deposition in kidneys and other organs and the sustained complement activation results in marked reduction in serum complement levels. High CRP levels were observed among the patient group contrary to the findings of *Li etal and were* correlating well with ds DNA antibody levels suggestive of active disease .*Pradhan etal*[13]had reported high CRP levels in north Indian lupus nephritis subjects and recent studies by *Eudy etal*[14]had reported a stronger association of CRP with flare in SLE subjects.

Conclusion

Systemic lupus patients presenting with Arthritic symptoms clinically resembles Rheumatoid Arthritis.In these Rheumatoid factor negative patients with suspected lupus arthritis, Anti nuclearAntibody, AntidsDNA Antibody can be used as diagnostic markers whereas complement levels can assess the disease activity. The inflammatory marker CRP was elevated in the patient group and needs further investigation to rule out infections or other inflammatory conditions as the role of CRP in active SLE or as a predictive disease activity marker is yet to be established. .High dsDNA titres along with elevated CRP might be useful in predictinglupus nephritis while hemoglobin levels and RDW are useful to detect anemia and chronic blood loss.Combined use of these biomarkers helps in early diagnosis and management and reduces the immune complex mediated injury to vital organs.

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