Original Research Article

A study of Anti Nuclear Antibody (ANA) in collagen vascular diseases

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Abstract

Background: The diagnosis of collagen vascular disease is based on clinical, serological and histological findings. The classical ANA indirect immunofluorescence assay is the most efficient screening test for LE.

Aim and objectives: To study ANA profile in various collagen vascular diseases.

Materials and methods: A study was conducted in 170 clinically confirmed cases of collagen vascular diseases during 2010-2012. A thorough clinical examination was carried out and baseline investigations were done. All the patients were subjected to complete ANA profile. Patients were followed up regularly in department of dermatology.

Results: Majority of the patients (55%) in our study were those of lupus erythematosus and systemic sclerosis (30%). The study revealed that 92% patients of SLE, 90% of MCTD, 85% of systemic sclerosis and 50% each of dermatomyositis and overlap syndromes showed ANA positivity. 77.14% and 42.85% patients of SLE showed anti Ds DNA and anti Ro 52 positivity respectively. Anti scl 70 positivity was seen in 75% patients of systemic sclerosis. All patients of MCTD tested positive anti u1 RNP.

Conclusion: ANA profile correlated very well with clinical manifestations in majority of patients in this study.

Key words

ANA, SLE, Systemic sclerosis, MCTD.

Introduction

Systemic collagen disorders refer to all inherited or acquired disorders of the connective tissue system. Lupus Erythematosus is characterized by reduced control of T-cells over the development of autoreactive B-cells, leading to formation of numerous non-organ specific autoantibodies. Production of autoantibodies in LE is time dependent: anti-nucleosome antibodies precede anti-DNA or anti-histone antibodies. Significant autoantibodies [1] in LE are as follows:

- Antinuclear antibody (ANA): The classical ANA indirect immunofluorescence assay is the most clinically efficient screening test for LE. Immunofluorescence patterns seen are Homogeneous, Speckled, Nucleolar, Peripheral and Centromeric.
- Anti ds-DNA antibody: Correlates well with disease activity and lupus nephritis
- Anti Sm antibody:Against Smith's antigen (spliceosome RNP).
- Anti U1-RNP antibody: suggest overlap, usually MCTD (100%).
- Antiribosomal-P antibody (rRNP): Highly specific for neuropsychiatric LE.
- Anti histone antibody:Seen in drug induced LE.
- Anti Ro antibody (Ssa) and Anti La antibody (SSb): more specific for SCLE and neonatal LE, Sjogren's syndrome.
- Anticardiolipin antibody: Best correlated with recurrent spontaneous abortions, thrombocytopenia, hypercoagulable state, false positive VDRL test, raised aPTT and neuropsychiatric LE.

Scleroderma

The common autoantibodies are [2]:
(a) ANA
(b)Anti-centromere antibody (CENP-B)
(c)Anti Scl-70 antibody (DNA topoisomerase I)
(d) RA factor positivity is roughly 25%.

Dermatomyositis [3]

Autoantibodies:
(a) ANA
(b)Myositis specific autoantibodies:
- Jo-1: histidyl tRNA synthetase; also seen in antisynthetase syndrome
- Mi-2: helicase nuclear proteins
- SRP: signal recognition peptide; s/o fulminant IIDM with cardiac involvement.

Mixed connective tissue disease [4]

A special form of overlap syndrome described by Sharpe in 1972 as a syndrome with overlapping features of systemic sclerosis, SLE and dermatomyositis associated with antibodies of RNAase sensitive extractable nuclear antigen. This ENA was subsequently characterized as the polypeptides on the U_1 ribonuclear protein component of the spliceosome (U_1-RNP)

Sjogren's syndrome [5]

Autoantibodies [6]
Anti-Ro SSA and Anti-La SSB

Rheumatoid arthritis [7]

RA Factor

Materials and methods

The present study of 170 cases of Collagen Vascular Diseases (CVDs) was carried out over a period of 2 years, 6 months (July 2010 to October 2012) at the Department of Dermatology. All patients presenting with history, symptoms and signs (with particular reference to clinical diagnostic criteria) suggestive of CVDs were included. A detailed history regarding the onset, duration and progress of mucocutaneous lesions and precipitating factors was noted. History pertaining to relevant systemic complaints, e.g. joint pain, muscular weakness, fever, dysphagia, dyspnoea, chest pain, edema, palpitation, any eye complaints or neuropsychiatric manifestations was actively

sought. In case of female patients, menstrual and obstetric history was noted. Complete general examination was carried out, followed by a thorough cutaneous examination from head to toe, including oral and genital mucosa.

Investigations [8]

All cases were subjected to baseline investigations. This comprised complete blood count with ESR, routine biochemistry panel (FBS, PPBS, RFT, LFT), urine routine and microscopic examination, serum proteins, X-ray chest, USG abdomen, ECG, RA factor, LE cell test. Punch biopsy was taken from the evident cutaneous lesions. Cases having signs and symptoms suggestive of SLE were subjected to ANA testing and anti-Ds DNA. Cases having

signs and symptoms suggestive of systemic sclerosis were subjected to barium swallow, barium meal follow-through and pulmonary function tests. Cases having signs and symptoms suggestive of dermatomyositis were subjected to serum creatine kinase levels, 24 hour urinary creatine levels and LDH. ENA profile was performed to confirm the MCTD cases.

Results and Discussion

In the present study of 170 cases of CVDs, 55% cases were of LE, 30% of scleroderma, 8 5% of dermatomyositis, 6% of mixed connective tissue disease and 4% cases of overlap syndromes (**Graph - 1**).

Graph – 1: Collagen vascular diseases.
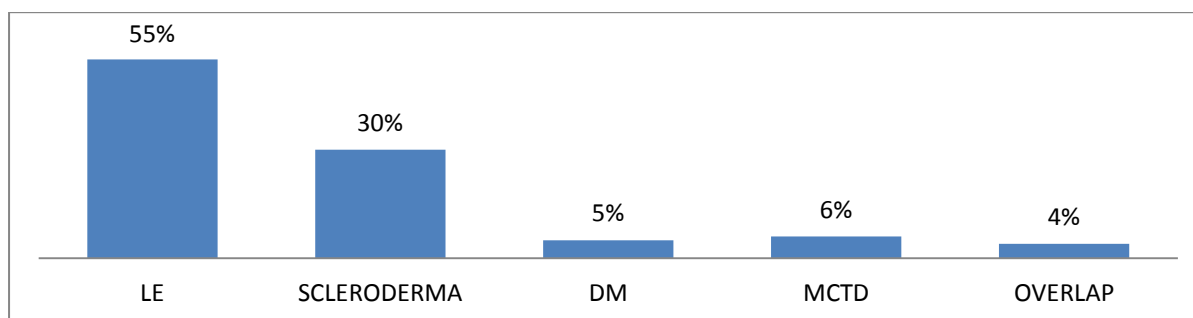
As seen in the table above, the highest incidence of CVDs was found in the age-group of 31-40 (18.23%), closely followed by 17.64% in the 21-30 years. There was a strong female preponderance (80%) across the study, bringing a female: male (F: M) ratio of 4: 1 (Male 20% and Female 80%) as per **Graph - 2**.

Lupus erythematosus

It was the single largest group. The various sub-groups were as follows:

Out of 93 cases of LE, there were 52 cases of SLE, 16 cases of DLE, 17 cases of DDLE, 6 cases of Rowell's syndrome and 2 cases of SCLE (**Graph – 3**).

The sex ratio of cases of LE in general was 3: 1 (**Table – 1**). An overwhelming majority of cases

of SLE were females and F: M ratio for SLE was 16: 1 as per **Table - 1**. This was consistent with the study Ghosh, et al. [9] which showed that in more females were affected at a ratio of 14 females to one male.

Out of 39 cases of SSc, 36 were females. Thus the F: M ratio was 12: 1. This ratio was almost identical to that reported by Sharma, et al. [10] and Usha, et al. [11] as per **Table – 2**.

ANA positivity was 92%.The commonest nuclear auto antibody was ant ds DNA (40% positivity). The commonest ANA pattern observed was homogeneous (**Graph – 4, 5**).
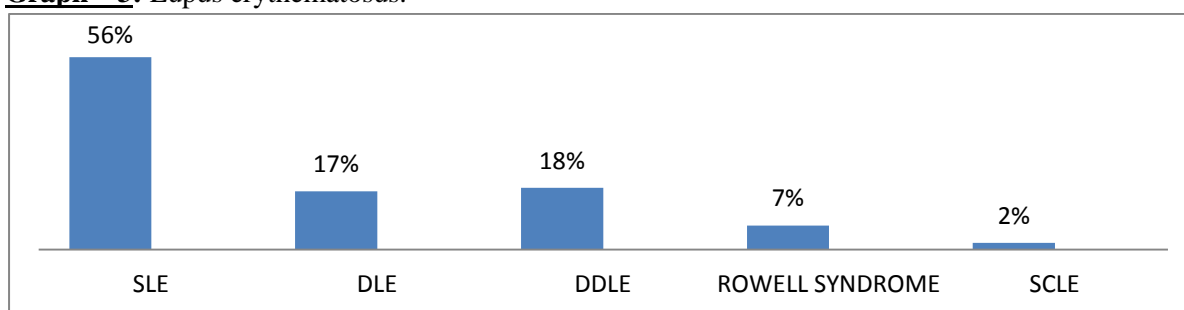
77.14% and 42.85% patients of SLE showed anti Ds DNA and anti Ro 52 positivity respectively.

Anti scl 70 positivity was seen in 75% patients of systemic sclerosis (**Graph – 6**). All patients of MCTD tested positive anti u1 RNP. Most commonly observed pattern was homogeneous.
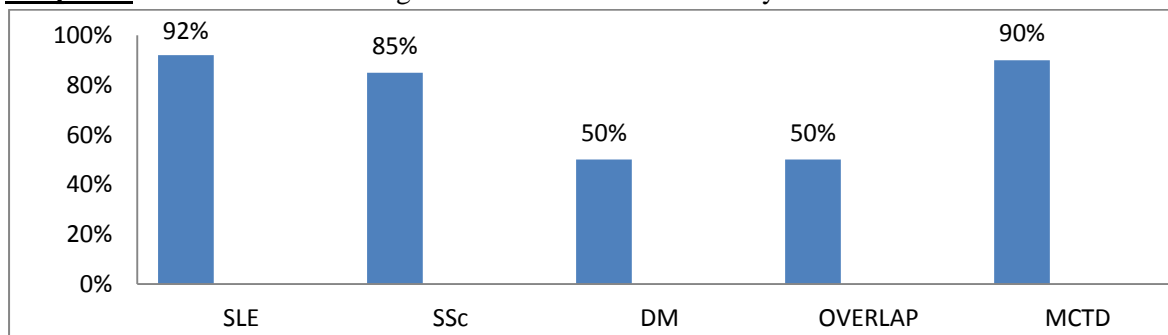
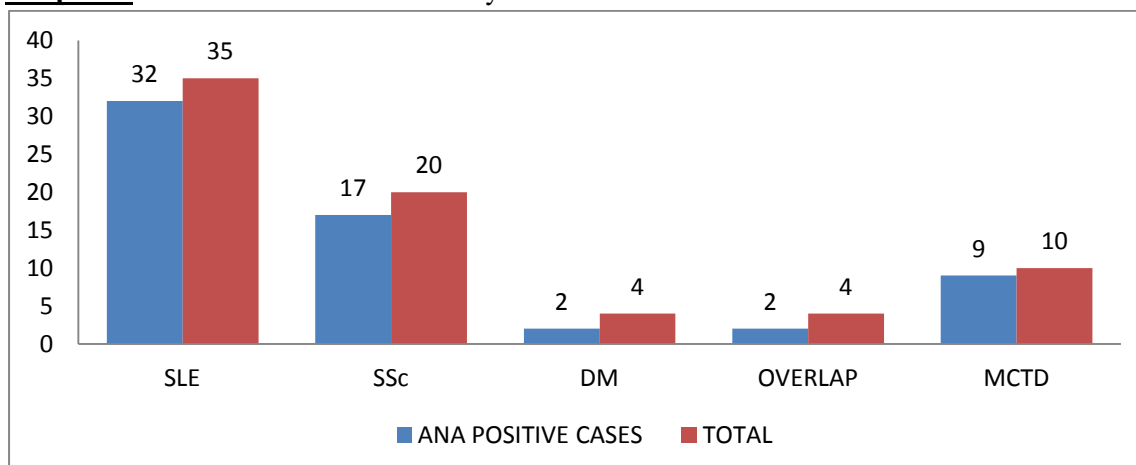**Graph – 2:** Age and sex distribution.
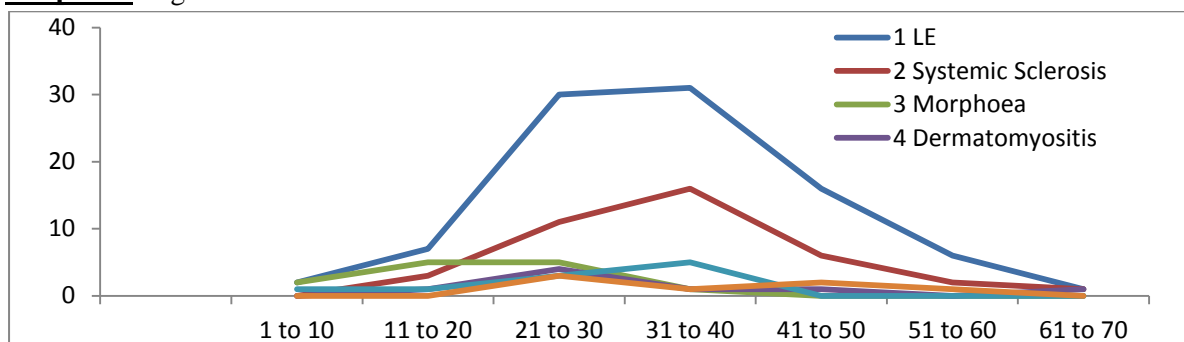
Graph – 3: Lupus erythematosus.

Graph – 4: No Of Cases Showing Positive Antinuclear Antibody.

Graph – 5: Positive Antinuclear antibody.

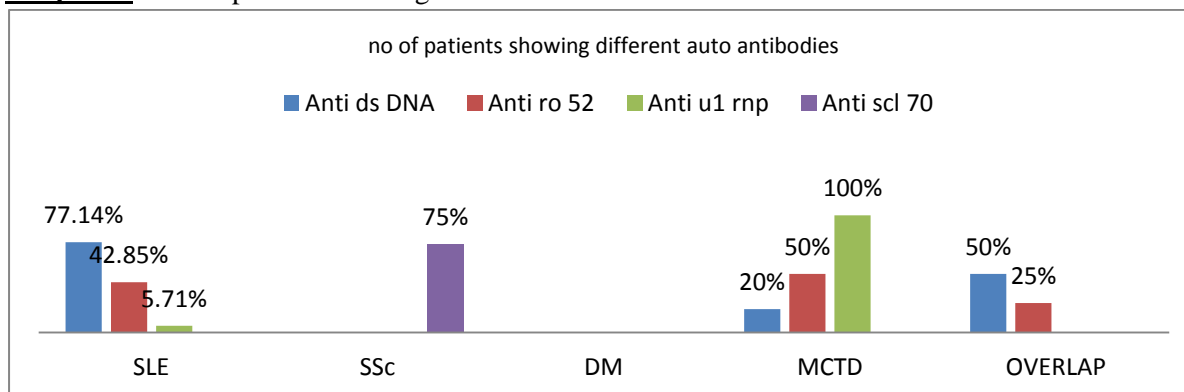**Graph – 6:** No. of patients showing different auto antibodies.

Table – 1: Sex distribution of various subsets of LE.

	Male	**Female**
SLE	3	49
DLE	9	7
DDLE	12	5
Rowell's	0	6
SCLE	0	2

Table – 2: Comparison of average age at presentation of systemic sclerosis.

Study	**Average age at presentation (years)**
Present	35
Sharma, et al. [10]	32.7
Usha, et al. [11]	36

Conclusion

ANA profile correlated very well with clinical manifestations in majority of patients in this study. Detection of ANAs by indirect immunofluorescence provides limited but clinically very useful information in absence of availability of direct immunofluorescence and electron microscopic studies. Serologic tests for autoantibodies are essential in the diagnosis and treatment of patients affected by collagen vascular disease. Those most commonly prescribed include antinuclear antibodies (ANA) and anti–double-stranded DNA antibodies (anti-dsDNA) [12, 13]. Antinuclear autoantibodies performed by indirect immunofluorescence is the first-level test advised for use in patients with symptoms and signs suggestive of autoimmune disease [12, 13].

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