MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.11.55.64

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Key Words
Systemic lupus erythematosus, sledai, hypocomplementemia, autoantibodies, disease activity, personalized therapy

Corresponding Author
Priyanka Priyadarshini Baishya,
Dept of Radiodiagnosis, Gauhati Medical College and Hospital, Guwahati, Assam, India

Author Designation
[1]Senior Resident
[2]Assistant Professor
[3]Professor
[4]Assistant Professor

Received: 25 September 2023
Accepted: 10 October 2023
Published: 11 October 2023

Citation: Sonali Dey, Diganta Das, Sanjeeb Kakati and Priyanka Priyadarshini Baishya, 2023. A Study of Antineutrophil Cytoplasmic Antibody Profile in Systemic Lupus Erythematosus Patients with Reference to Disease Activity and Organ Involvement. Res. J. Med. Sci., 17: 55-64, doi: 10.59218/makrjms.2023.11.55.64

A Study of Antineutrophil Cytoplasmic Antibody Profile in Systemic Lupus Erythematosus Patients with Reference to Disease Activity and Organ Involvement

[1]Sonali Dey, [2]Diganta Das, [3]Sanjeeb Kakati and [4]Priyanka Priyadarshini Baishya

[1]Department of Rheumatology, IPGMER, Kolkata, India
[2,3]Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, India
[4]Department of Radiodiagnosis, Gauhati Medical College and Hospital, Guwahati, Assam, India

ABSTRACT
Systemic lupus erythematosus (SLE) is characterized by a diverse array of clinical presentations, warranting comprehensive analyses to decipher the potential correlations between disease activity scores, complement levels and autoantibodies prevalence. In this cross-sectional study spanning a period of 12 months, we investigated the correlation between disease activity, hypocomplementemia and various autoantibodies in 200 patients with systemic lupus erythematosus (SLE) at a tertiary healthcare center. Utilizing various clinical and laboratory markers, we aimed to construct a detailed understanding of the disease patterns and manifestations, which might foster more precise management and intervention strategies for individuals afflicted with SLE. A significant segment of the study population showcased moderate to high disease activity, with 37.50% displaying SLEDAI scores between 11-20. A notable correlation was observed between low complement C3 levels and the presence of dsDNA antibodies (77.7%). Moreover, the presence of anti-dsDNA was significantly associated with higher disease activity scores, reaffirmed by a p-value of 0.007. The findings underscore the pivotal role of complement levels and specific autoantibodies as potential markers for monitoring disease activity in SLE patients. These parameters could potentially guide the development of personalized therapeutic strategies, fostering improved management of SLE.

INTRODUCTION

Systemic lupus erythematosus (SLE), a chronic and complex autoimmune disorder characterized by the inflammation of various organs and tissues, is notorious for its heterogeneous clinical manifestations and unpredictable course[1,2]. The disease predominantly affects women in their reproductive years, imposing a considerable burden on healthcare systems and affecting the quality of life of the patients[3]. One pivotal area of research in understanding and managing SLE has been the exploration of various autoantibodies that play an intricate role in the pathogenesis of the disease, including the antineutrophil cytoplasmic antibodies (ANCA) which are the focal point of this investigation. The profile of ANCA in SLE patients, in reference to disease activity and organ involvement, remains an area warranting in-depth research to augment our understanding of the SLE complex pathobiology[4,5].

Traditionally, ANCAs have been profoundly associated with ANCA-associated vasculitides (AAV), where they serve as significant biomarkers for diagnosis and monitoring of disease activity[6]. However, over recent years, the occurrence of ANCAs in patients with SLE and its potential correlation with disease activity and specific organ involvement has emerged as a subject of considerable interest[7]. ANCA in SLE patients has been hypothesized to be associated with a more severe disease phenotype, with particular reference to renal and neuropsychiatric involvement, though the data are somewhat conflicting, necessitating further studies in this direction[8,9].

The ANCA profile in SLE is typically diverse, with a majority of studies focusing on the prevalence of atypical ANCAs, predominantly perinuclear ANCAs (p-ANCAs) and its variants targeting multiple antigens such as lactoferrin and elastase[10,11]. The mechanism of ANCA-induced injury in SLE is thought to involve a complex interaction between ANCAs and neutrophils, culminating in endothelial damage and subsequent organ involvement, thereby possibly serving as a surrogate marker for disease activity[12,13].

Moreover, the potential role of ANCAs in predicting the disease course and organ involvement in SLE could have significant implications for personalizing treatment strategies. An enhanced understanding of the ANCA profile could pave the way for the development of targeted therapies aimed at modulating the ANCA-neutrophil axis, potentially leading to improved outcomes for SLE patients[14,15].

Furthermore, it is also pertinent to delve into the diagnostic conundrum that ANCA presents in SLE. The coexistence of ANCAs and other autoantibodies, like anti-double-stranded DNA (anti-dsDNA), may result in a complex clinical presentation, often blurring the lines between SLE and other autoimmune disorders, making differential diagnosis a challenging endeavor[16]. Hence, an exhaustive exploration into the ANCA profile could potentially offer clarity in delineating SLE from other ANCA-associated disorders, thereby facilitating more accurate diagnoses and better clinical management[17,18].

To formulate a more definitive standpoint on the role of ANCAs in SLE, it becomes essential to undertake studies that encompass a broader spectrum of clinical and laboratory parameters. These should aim at investigating the relationship between ANCAs and various clinical manifestations, disease activity scores and laboratory markers in SLE patients to provide a more comprehensive insight into the role of ANCAs in the pathophysiology of SLE[19].

Furthermore, understanding the genetic and environmental factors that influence the production of ANCAs in SLE might offer novel insights into disease susceptibility and progression, potentially guiding the development of new therapeutic strategies[20,21].

Given the complexity of SLE and the potential implications of ANCA profiling in understanding disease progression and management, this study seeks to elucidate the ANCA profile in SLE patients, particularly focusing on its association with disease activity and organ involvement. Such an endeavor is expected to not only enrich the existing body of knowledge but may also lay the foundation for innovative therapeutic approaches, fostering improved patient outcomes.

In light of the aforementioned perspectives, this study aims to comprehensively analyze the ANCA profile in SLE patients with meticulous reference to disease activity and organ involvement. Through this endeavour, we anticipate fostering a richer understanding of SLE's intricate pathobiology and thereby contributing to more nuanced, patient-centric clinical management strategies.

Aims and objective:

- To study antineutrophil cytoplasmic antibody (ANCA) positivity in systemic lupus erythematosus patients
- To study association of antineutrophil cytoplasmic antibody (ANCA) in systemic lupus erythematosus patients with reference to organ involvement and disease activity

MATERIALS AND METHODS

Study setting: The study was carried out at the Department of Medicine, Assam Medical College and Hospital, Dibrugarh, Assam, a recognized institution known for its robust healthcare facilities and expert personnel.

Study design: This research is a hospital-based cross-sectional observational study aimed at investigating the presence of antineutrophil cytoplasmic antibody (ANCA) in patients diagnosed with systemic lupus erythematosus (SLE) and examining its relation to disease activity and organ involvement.

Duration of study: The study spanned one year, starting from July 2017 and concluding in June 2018.

Study population: The research encompassed all consecutive cases of SLE patients who were attending the Rheumatology Outpatient Department (OPD) or other outpatient departments or were admitted in various wards of the Department of Medicine and Dermatology at Assam Medical College and Hospital.

Inclusion criteria:

- All SLE patients who were attending the Rheumatology OPD or other outpatient departments or staying in various wards of the Department of Medicine and Dermatology at Assam Medical College and Hospital and who met the criteria as per the Systemic Lupus International Collaborating Clinics (SLICC) criteria, established in 2012
- Patients aged 13 years and above

Exclusion criteria: The following categories of individuals were excluded from the study:

- Individuals aged below 13 years
- Patients who refused to give consent for participation
- Cases of drug-induced lupus

Sampling method: The sample size for the study was determined using the equation

$$\frac{4PQ}{d^2}$$

Where:

P = Anticipated proportion (14% or 0.14 as per a previous study by Zhan *et al*.[22]
Q = 100-P (or 0.86)
d = Allowable error (0.05)

Using this equation, a sample size of approximately 193 was derived, which was later rounded off to 200 to account for potential data loss or exclusions.

Data collection: Patients were identified based on the SLICC criteria for the classification of SLE (2012), which stipulates that a patient must satisfy four of the designated criteria, including at least one clinical criterion and one immunologic criterion, or present with biopsy-proven nephritis compatible with SLE along with ANA or anti-dsDNA antibodies.

Statistical analysis: Statistical analysis was conducted to represent the results in terms of percentage and mean ± standard deviation (SD). To ascertain the statistical significance between the presence of autoantibodies, clinical symptoms and disease activity, Chi-square tests and Fisher's exact test were applied where necessary. A p-value of ≤ 0.05 was considered to indicate statistical significance.

Ethical considerations: All participants provided informed consent before their inclusion in the study and all procedures were conducted in accordance with the ethical standards of the institutional research committee.

RESULTS

In the study conducted to assess the incidence of antineutrophil cytoplasmic antibody (ANCA) in systemic lupus erythematosus (SLE) patients, a significant amount of data was collected to better understand the demographic and clinical characteristics of the population studied.

From the total participants, the majority belonged to the age group of 20-30 years, representing 43.5% of the study population, followed by the age group of 30-40 years which constituted 31.5%. The least represented were individuals above 50 years, comprising a mere 0.5% of the study population, indicating that SLE is noticeably less prevalent in this age bracket or it may suggest a younger cohort within the study settings (Table 1).

In terms of gender distribution, a striking majority were females, making up 95% of the population, which mirrors the general tendency of SLE affecting females more predominantly compared to males. This gender disparity is a vital finding, which points towards a possible genetic or hormonal role in the manifestation of the disease.

When examining the types of symptoms exhibited by the participants, mucocutaneous symptoms were most commonly reported, with a prevalence of 93%, followed by renal and constitutional symptoms which were reported in 79 and 77.5% of the cases respectively. The least prevalent were cardiovascular symptoms at 13.5%. These findings reflect the multi-organ involvement nature of SLE, with varying degrees of manifestations.

In regard to the antinuclear antibody (ANA) test results, an overwhelming majority of 99% were found to be positive. This indicates a strong presence of these

Table 1: Demographic and clinical characteristics of SLE patients

Characteristics	No.	Percentage
Age		
13 -<20	39	19.5
20 -<30	87	43.5
30 -<40	63	31.5
40 -<50	10	5.0
≥50	1	0.5
Sex		
Female	190	95.0
Male	10	5.0
Types of symptoms		
Mucocutaneous	186	93.0
Renal	158	79.0
Constitutional	155	77.5
Musculoskeletal	132	66.0
Hematological	130	65.0
Neuropsychiatric	91	45.5
Gastrointestinal	71	35.5
Respiratory	51	25.5
Vasculitis	54	27.0
Serositis	37	18.5
Cardiovascular	27	13.5
Antinuclear antibody		
Positive	198	99.0
Negative	2	1.0
Duration of disease (years)		
<1	108	54.0
1–<2	38	19.0
2–<3	18	9.0
3–<4	12	6.0
4–<5	6	3.0
≥5	18	9.0

Table 2: Antineutrophil cytoplasmic antibody (immunofluorescence assay)

Antineutrophil cytoplasmic antibody	No.	Percentage
Positive		
pANCA	53	26.5
cANCA	2	1.0
Negative	145	72.5
Total	200	100.0

antibodies in SLE patients, making it a potentially reliable marker for diagnosis and tracking disease progression.

Lastly, analyzing the duration of the disease in the study population, over half (54%) were found to be in the initial year of their disease journey, highlighting a substantial number of newly diagnosed cases. The number gradually decreases as the duration increases, with only 3% having a duration of 4 to less than 5 years and an uptick observed in patients with a disease duration of 5 years or more at 9%.

Overall, the data reflects the complexity and varied presentation of SLE, emphasizing the necessity for a multifaceted approach in the management and study of this disease. Further studies can delve deeper into understanding the correlations between the demographic factors and the type and severity of symptoms, which can aid in developing targeted treatment strategies and enhancing patient care.

Table 2 showcases the distribution of antineutrophil cytoplasmic antibodies (ANCA) amongst the studied SLE patients using an immunofluorescence assay. The analysis reveals that a subset of the study population tested positive for ANCA with variations in their distribution-perinuclear (pANCA) and cytoplasmic (cANCA) patterns.

Of the total sample population, 26.5% (53 individuals) demonstrated pANCA positivity, indicating that a significant portion of SLE patients had these antibodies present. Notably, the prevalence of cANCA was considerably lower, with only 1% (2 individuals) showcasing positivity. These data suggest that pANCA is more commonly associated with SLE patients compared to cANCA, which might imply a certain degree of specificity in the manifestation of SLE.

On the contrary, a majority of the study population, 72.5% (145 individuals), did not exhibit any ANCA positivity, highlighting that while ANCA can be present in a significant subset of SLE patients, its absence is still more common, suggesting it might not be a principal marker for SLE. Therefore, while ANCAs may contribute to the pathological mechanisms of SLE, their presence might not be universally observed across all individuals with the condition.

In sum, this table delineates a distinct occurrence of ANCAs, particularly pANCAs, in a noticeable portion of SLE patients, offering potential insights into the heterogeneity of the disease and possibly paving the way for future investigations into the role of ANCAs in SLE. It might be beneficial to further explore how the presence of these antibodies correlates with disease activity, clinical manifestations and outcomes to provide a more comprehensive understanding of SLE. It may also encourage the development of more targeted diagnostic criteria and therapeutic approaches, catering to the individual needs and conditions of SLE patients.

Table 3 illustrates the relationship between the presence of Antineutrophil Cytoplasmic Antibody (ANCA) and the occurrence of various other antibodies in patients with SLE.

A significant association is apparent between ANCA positivity and the presence of Anti-ds DNA, Anti-Nucleosome and Antihistone antibodies, with p-values of 0.04, 0.00 and 0.003, respectively. Around 80% of ANCA-positive patients were found to have Anti-ds DNA antibodies compared to approximately 64.14% in the ANCA-negative group, indicating a significant correlation between these antibodies and ANCA positivity. Furthermore, a substantial proportion of ANCA-positive patients demonstrated Anti-Nucleosome (49.10%) and Antihistone (54.55%) antibodies, as opposed to markedly lower percentages in the ANCA-negative group, 17.93 and 31.03% respectively, showcasing a significant discrepancy and suggesting a potential linkage between the presence of these antibodies and ANCA positivity.

On the other hand, other antibodies such as Anti-SmD1, Anti-PCNA, Anti-Ribosomal P, Anti-Ro (60kDa and 52kDa), Anti-La, AntiCENP B, Anti-Scl 70, Anti-U1 snRNP, AMA M2, Anti-jo 1, Anti-Pm Scl, Anti-Mi 2 and Ku did not exhibit a significant association

Table 3: Association of antineutrophil cytoplasmic antibody (ANCA) with other antibodies

Other antibodies	ANCA positive n = 55 (%)	ANCA negative n = 145 (%)	p-value
Anti ds DNA	44 (80)	93 (64.14)	0.040
Anti Nucleosome	27 (49.10)	26 (17.93)	0.000
Antihistone	30 (54.55)	45 (31.03)	0.003
Anti SmD1	20 (36.36)	40 (27.58)	0.230
Anti PCNA	4 (7.27)	10 (6.9)	1.000
Anti Ribosomal P	15 (27.27)	40 (27.59)	1.000
Anti Ro (60kDa)	26 (47.28)	73 (50.34)	0.750
Anti Ro (52kDa)	19 (34.55)	55 (37.55)	0.740
Anti La	9 (16.37)	23 (15.86)	1.000
AntiCENP B	0	2 (1.37)	1.000
Anti Scl 70	0	3 (24)	0.560
Anti U1 snRNP	9 (16)	21 (14.48)	0.820
AMA M2	1 (1.82)	6 (4.14)	0.670
Anti jo 1	0	0	1.000
Anti Pm Scl	1 (1.82)	3 (20.69)	1.000
Anti Mi 2	1 (1.82)	1 (0.69)	0.470
Ku	1 (1.82)	1 (0.69)	0.470

with ANCA status, as indicated by p-values greater than 0.05. These antibodies were observed in both ANCA-positive and ANCA-negative groups with no considerable difference in their proportions, implying that they might not have a direct correlation with ANCA positivity.

In conclusion, this table reveals significant associations between ANCA positivity and specific antibodies (Anti-ds DNA, Anti-Nucleosome and Antihistone), hinting at potential pathways or mechanisms that might be operating in SLE patients. These findings might be instrumental in unraveling the complexity of the immunological aspects of SLE, potentially aiding in devising more nuanced diagnostic criteria or therapeutic strategies. Further research might be warranted to explore these relationships in depth and elucidate the underlying mechanisms driving these associations, which could pave the way for more targeted and effective interventions in the management of SLE.

Table 4 sheds light on the various clinical manifestations observed in patients with ANCA positive and ANCA negative statuses, examining a broad range of symptoms categorized under headings such as constitutional symptoms, mucocutaneous manifestations, musculoskeletal manifestations and several others.

From the constitutional symptoms category, fever seems to have a significant association with ANCA positivity with 70.91% of ANCA positive patients reporting fever compared to only 37.9% in ANCA negative patients, denoted by a p-value of 0. This significant correlation extends to symptoms such as malaise, anorexia and lymphadenopathy as well with p-values of 0.017, 0.004 and 0.004, respectively, indicating a high prevalence in ANCA positive patients. Under mucocutaneous manifestations, it is noteworthy that while some symptoms like pigmentation and alopecia have a nearly equal prevalence in both groups (with p-values of 0.87 and 1, respectively), mucosal ulcers were more frequent in ANCA positive patients with a noticeable p-value of 0.07. However, no significant difference was found in the prevalence of other symptoms in this category between the two groups.

When considering musculoskeletal manifestations, arthralgia or arthritis was a common finding in both groups with no significant difference (p-value: 0.74). The neurological manifestations section indicates that most symptoms are somewhat evenly distributed between the two groups, with no substantial difference in prevalence.

In terms of renal manifestations, there is a significant difference between the two groups. For instance, oliguria or anuria and raised serum creatinine levels (>1.4 mg dL^{-1}) were notably higher in ANCA positive patients with p-values of 0.016 and 0, respectively. Proteinuria, too, had a strong association with ANCA positivity, seen in 90.9% of ANCA positive patients as opposed to 68.96% in the ANCA negative group, with a p-value of 0.001.

Serositis manifested as ascites was more common in ANCA positive patients, shown by a p-value of 0.014. Vasculitis, characterized by Raynaud's phenomenon and palpable purpura, was significantly more prevalent in ANCA positive patients, indicated by p-values of 0.0006 and <0.00001 respectively.

Cardiovascular manifestations like palpitation were more prevalent in ANCA positive patients (p-value: 0.003) and in hematological manifestations, thrombocytopenia and leucopenia were significantly associated with ANCA positivity, as evidenced by p-values of 0.0005 and 0.0024, respectively.

Gastrointestinal manifestations revealed dyspepsia or peptic ulcer disease and pancreatitis were more common in ANCA positive patients, with respective p-values of 0.01 and 0.049. Pleuropulmonary manifestations like pneumonia also appeared more frequently in ANCA positive patients (p-value: 0.02).

Table 5 displays the distribution of disease activity scores according to the systemic lupus erythematosus disease activity index (SLEDAI) across a study population of 200 individuals.

Table 4: Clinical manifestations in ANCA positive and negative patients

Clinical manifestations	ANCA positive n = 55 (%)	ANCA negative n = 145 (%)	p-value
Constitutional symptoms			
Fever	39 (70.91)	55 (37.9)	0
Fatigue	41 (74.55)	89 (61.38)	0.09
Malaise	36 (65.45)	66 (45.52)	0.017
Anorexia	28 (50.91)	41 (28.27)	0.004
Lymphadenopathy	5 (9.1)	6 (4.14)	0.004
Mucocutaneous manifestations			
Malar rash	16 (29.1)	42 (28.96)	0.82
Discoid rash	12 (21.82)	19 (13.1)	0.13
SCLE	2 (3.63)	12 (8.27)	0.36
Photosensitivity	38 (69.1)	89 (61.38)	0.33
Pigmentation	31 (56.36)	79 (54.48)	0.87
Scaling	9 (16.36)	13 (8.96)	0.2
Mucosal ulcer	20 (36.36)	34 (23.49)	0.07
Alopecia	35 (63.64)	93 (64.14)	1
Musculoskeletal manifestations			
Muscle tenderness	5 (9.09)	10 (6.89)	0.56
Muscle weakness	7 (12.72)	15 (10.34)	0.62
Arthralgia/arthritis	36 (65.45)	90 (62.07)	0.74
Neurological manifestations			
Lupus Headache	18 (32.73)	43 (29.65)	1
Psychosis	6 (10.91)	10 (6.89)	0.38
Seizure	6 (10.91)	10 (6.89)	0.38
Cranial Nerve Disorder	1 (1.82)	0	0.28
Peripheral Neuropathy	9 (16.36)	23 (15.86)	1.00
Spinal cord lesion (transverse myelitis)	1 (1.82)	0	0.27
CVA	1 (1.82)	1 (0.69)	0.47
Visual disturbance	2 (3.63)	10 (6.89)	0.52
Cognitive symptoms	2 (3.63)	1 (0.69)	0.18
Renal manifestations			
Oliguria/anuria	20 (36.36)	1 (0.69)	0.016
Facial puffiness/edema	24 (43.64)	41 (28.27)	0.04
Hematuria	4 (7.27)	6 (4.14)	0.47
Active urinary cast	9 (16.36)	7 (4.83)	0.016
Raised serum creatinine (>1.4 mg dL^{-1})	19 (34.5)	13 (8.96)	0
Proteinuria (>0.5 g/24 hrs)	50 (90.9)	100 (68.96)	0.001
Serositis			
Pleural effusion	9 (16.36)	14 (9.65)	0.216
Pericardial Effusion	11 (20)	13 (8.96)	0.048
Ascitis	12 (21.82)	12 (8.27)	0.014
Vasculitis			
Raynaud's phenomenon	15 (27.27)	11 (7.58)	0.0006
Palpable purpura	28 (50.91)	10 (6.89)	<0.00001
Gangrene	2 (3.64)	1 (0.69)	0.183
Cardiovascular manifestations			
Palpitation	9 (16.36)	5 (3.45)	0.003
Hypertension	9 (16.36)	11 (7.58)	0.11
Valvular abnormality	0	2 (1.38)	1
Hematological manifestations			
Anaemia	40 (72.73)	85 (58.62)	0.07
Thrombocytopenia	10 (18.18)	4 (2.76)	0.0005
Leucopenia	10 (18.18)	6 (4.14)	0.0024
Gastrointestinal manifestations			
Hepatomegaly	8 (14.54)	14 (9.65)	0.32
Splenomegaly	1 (1.82)	11 (7.58)	0.18
Dyspepsia/Peptic ulcer disease	12 (21.82)	11 (7.58)	0.01
Pancreatitis	4 (7.27)	2 (1.38)	0.049
Jaundice/Hepatitis	3 (5.45)	0	0.02
Pleuropulmonary manifestations			
Pneumonia	16 (29.10)	21 (14.48)	0.02
Pleuritis	9 (16.36)	22 (15.17)	0.829
Alveolar hemorrhage	2 (3.64)	0	0.07

Table 5: Disease activity score

Disease activity score (SLEDAI)	No.	Percentage
0–10	66	33.00
11–20	75	37.50
21–30	43	21.50
31–40	10	5.00
41–50	4	2.00
>50	2	1.00
TOTAL	200	100.00
Mean±S.D	----------16.27±9.83 ----------	
Median	----------14 ----------	

A significant proportion of patients have a moderate level of disease activity, with 37.5% having a score ranging from 11-20. Following closely, 33% of patients exhibit mild disease activity with scores ranging between 0 and 10. There is also a considerable group, constituting 21.5%, who are experiencing a higher level of disease activity, with scores falling in the range of 21-30. A small portion of the population experiences even more severe levels of disease activity, with 5% having scores between 31 and 40 and a combined 3% having scores of 41 or above, indicating extremely severe disease manifestations.

Regarding the central tendency measures, the mean SLEDAI score in this cohort is 16.27 with a standard deviation of 9.83, suggesting a moderate

Table 6: Relationship of hypocomplementemia with sledai score

	Low complement C3 (<90 mg dL^{-1})		Low complement C4 (<9 mg dL^{-1})		Both low C3 and C4	
SLEDAI scores	n = 117	Percentage	n = 52	Percentage	n = 50	Percentage
0-10	16	13.68	7	13.46	6	12
11-20	50	42.70	22	42.30	21	42
21-30	35	29.90	14	26.90	14	28
31-40	10	8.55	7	13.46	7	14
41-50	4	3.40	2	7.69	2	4
>50	2	1.70	0	0.00	0	0

Table 7: Relationship of disease activity score (sledai) with different autoantibodies

	SLEDAI score (0-10) n = 66 (%)		SLEDAI score (11-20) n = 75 (%)		SLEDAI score (21-30) n = 43 (%)		SLEDAI score (>30) n = 16 (%)		
Autoantibodies	No.	Percentage	No.	Percentage	No.	Percentage	No.	Percentage	p value
ANCA	8	12.1	19	25.3	19	44.2	9	56.2	0.00
Anti dsDNA	35	53.0	55	73.3	33	76.7	14	87.5	0.007
Anti Sm	17	25.8	22	29.3	11	25.6	10	62.5	0.039
Antihistone	19	28.8	29	38.7	17	39.5	10	62.5	0.09
Antinucleosome	5	7.6	23	30.7	17	39.5	8	50.0	0.00
Anti Ro 60 kDa	30	45.4	37	49.3	21	48.8	11	68.7	0.42
Anti Ro 52 kDa	28	42.4	22	29.3	15	34.8	9	56.2	0.14
Anti Ribosomal P	16	24.2	17	22.7	15	34.8	7	43.7	0.25
Anti U1sn RNP	8	12.1	11	14.7	5	11.6	6	54.5	0.06
Anti La	8	12.1	13	17.3	9	20.9	2	18.2	0.62

average level of disease activity with a fair amount of variability in scores. The median score of 14 indicates that over half of the population has a SLEDAI score of 14 or less, pointing towards a data distribution that leans slightly towards the lower end of the disease activity spectrum.

The insights derived from this table can be instrumental in understanding the overall disease activity landscape in this population. This data helps in portraying a clearer picture of the severity spectrum of the disease across this cohort, which may guide in developing individualized treatment plans and optimizing healthcare resource allocation. Furthermore, it can be a valuable asset in academic research, exploring correlations between disease activity levels and various clinical outcomes or manifestations.

In Table 6, we explore the relationship between varying levels of disease activity (as categorized by the SLEDAI score) and the incidence of hypocomplementemia, characterized by low levels of complement proteins C3 and C4 in the blood. These complements are typically decreased in systemic lupus erythematosus (SLE) and are markers of disease activity.

A glance at the data reveals that a substantial portion of patients with SLEDAI scores ranging from 11 to 20 exhibit hypocomplementemia, with 42.7% having low levels of Complement C3, 42.3% showcasing low levels of Complement C4 and 42% displaying reduced levels of both complements.

Patients with a SLEDAI score between 21 and 30 also have a notable incidence of hypocomplementemia, constituting 29.9% (low C3), 26.9% (low C4) and 28% (low C3 and C4) of the respective categories. It seems that as the SLEDAI score increases, there's a notable but not proportionate increase in the percentage of patients with hypocomplementemia, especially regarding those with low levels of both complements.

Moreover, the data shows that even patients with mild disease activity (SLEDAI score 0-10) experience hypocomplementemia, albeit at a lower percentage compared to groups with higher disease activity scores. It is also significant that in the most severe category (SLEDAI score >50), the data indicates no patients exhibited low levels of Complement C4 or both C3 and C4, though this group represents a very small portion of the population.

In terms of individuals with high disease activity (SLEDAI score 31-50), the percentage of those with hypocomplementemia varies between 3.4-8.55% for low C3 and 7.69-13.46% for low C4, displaying a possible non-linear relationship between disease activity and hypocomplementemia.

This table illustrates a complex relationship between SLEDAI scores and complement levels, indicating that while there seems to be a correlation, it may not be strictly linear and other factors could be influencing complement levels in these patients. This information could be beneficial in enhancing the understanding of the pathophysiological mechanisms underlying SLE and in the formulation of targeted therapeutic strategies.

Table 7 presents the relationship between the disease activity score (SLEDAI) and different autoantibodies observed in the study.

The ANCA antibody shows a significant correlation with the SLEDAI score, with a notable increase in percentage as the score escalates, indicating a higher disease activity at elevated scores. This trend is notably clear, as seen from a 12.1% prevalence at scores between 0 and 10-6.2% prevalence at scores above 30, with a p-value of 0.00, signifying this relationship is statistically significant.

Table 8: Relationship of hypocomplementemia (low complement c3 level) with different autoantibodies

	Low C3 (<90 mg dL^{-1}) n = 117 (%)		Normal C3 (≥90 mg dL^{-1}) n = 83 (%)		
Autoantibodies	No.	Percentage	No.	Percentage	p-value
ANCA	37	31.6	11	13.2	0.003
dsDNA	91	77.7	46	55.4	0.001
Anti SmD1	42	35.9	18	21.7	0.030
Anti nucleosome	44	37.6	9	10.8	0.000
Anti Ro (60 kDa)	55	47.0	44	53.0	0.400
AntiRo (52 kDa)	39	33.3	35	42.2	0.200
Anti ribosomal P	34	29.0	21	25.3	0.560
Anti La	17	14.5	15	18.0	0.500
Antihistone	52	44.4	23	27.7	0.020
Anti U1 RNP	23	19.6	7	8.4	0.003

Similarly, the Anti dsDNA antibody displays an escalating trend, demonstrating an increasing presence from 53.0% at the lowest score range to 87.5% at scores above 30. This pattern, supported by a p-value of 0.007, suggests a significant association between the presence of this antibody and higher disease activity scores.

The presence of Anti Sm antibodies also shows a substantial increase in higher score categories, notably jumping from 25.8% in the 0-10 score range to 62.5% in the above 30 score range. This association is proven to be statistically significant with a p-value of 0.039.

Meanwhile, the Antihistone and Antinucleosome antibodies reveal significant variations across the different score categories, with respective p-values of 0.09 and 0.00. Particularly, the Antinucleosome antibodies demonstrate a steep increase from 7.6-50% as we move from the lower to the higher SLEDAI scores, showcasing its potential role in disease activity. The remaining antibodies, such as Anti Ro (60kDa and 52kDa), Anti Ribosomal P, Anti U1sn RNP and Anti La, also exhibit varying percentages across different score categories, albeit with larger p-values, which might indicate a less prominent relationship with the SLEDAI scores in this study population.

Overall, the table portrays intricate connections between various autoantibodies and the SLEDAI scores, providing a vista to understand the immunological landscape in SLE and its relation with disease activity.

In Table 8, the relationship between hypocomplementemia, specifically low levels of complement C3 and various autoantibodies is examined.

Analyzing the data for the ANCA antibody, we see a significant prevalence among individuals with low C3 levels, registering at 31.6%, compared to a much lower 13.2% in individuals with normal C3 levels. This relationship is statistically significant, as evidenced by a p-value of 0.003.

Similarly, the dsDNA antibody displays a markedly higher prevalence in the low C3 group (77.7%) compared to the normal C3 group (55.4%), with a p-value of 0.001 indicating a significant association between low C3 levels and the presence of this antibody.

A closer look at the Anti SmD1 antibody reveals a significant association with low C3 levels as well, with a higher prevalence noted in the low C3 group (35.9%) compared to the normal C3 group (21.7%). The relationship is statistically significant with a p-value of 0.03.

The anti nucleosome antibody stands out with a very pronounced difference in prevalence between the groups. A significant 37.6% of individuals in the low C3 group tested positive for this antibody, in contrast to only 10.8% in the normal C3 group. This stark difference is confirmed as statistically significant with a p-value of 0.00.

The data for antibodies Anti Ro (60 and 52 kDa), Anti Ribosomal P and Anti La show variations in prevalence between the two groups, however, with p-values of 0.40, 0.20, 0.56 and 0.50, respectively, these differences are not statistically significant.

In contrast, the Antihistone antibody shows a significant relationship with C3 levels, with a higher prevalence noted in the low C3 group (44.4%) compared to the normal C3 group (27.7%). This association has a p-value of 0.02, establishing its statistical significance.

Lastly, the Anti U1 RNP antibody also shows a significant relationship with C3 levels, with a higher frequency of 19.6% in the low C3 group compared to 8.4% in the normal C3 group, supported by a p-value of 0.003, confirming a statistically significant relationship. Overall, this table provides a comprehensive view of the relationship between various autoantibodies and low complement C3 levels, highlighting potential pathways of immune involvement in the pathophysiology of SLE.

DISCUSSIONS

In the evaluation of disease activity scores delineated through SLEDAI, it has been observed that a significant segment of the studied population exhibits moderate to high disease activity, mirroring the trends observed in several other cohorts. This segment of the patient population showcases scores ranging from 11-20, indicating the persistent nature of moderate disease activity in a substantial portion of individuals with SLE. Such observations align well with the studies conducted by Petri *et al*.[23] wherein a direct correlation

between disease activity and the SLEDAI scores was established, emphasizing the necessity for comprehensive management strategies to mitigate the risks associated with higher disease activity levels.

Furthermore, hypocomplementemia, characterized by low complement levels C3 and C4, presents as a significant marker for disease activity in SLE, a finding substantiated by several studies in the literature. These studies elucidate a clear correlation between diminished complement levels and increased disease activity, hinting at the critical role these complement levels potentially play in disease progression. In fact, Tsokos[1] illustrated that complement activation products might serve as markers of disease activity, thereby potentially guiding therapeutic strategies for individuals presenting with varied SLEDAI scores.

The analysis also draws attention to the relationship between various autoantibodies and the SLEDAI scores. In this regard, anti-dsDNA antibodies have been prominently associated with higher SLEDAI scores. This observation is in line with the work of Swaak *et al*.[24], which documented a clear correlation between the presence of these antibodies and a marked increase in disease activity, thereby underlining the predictive role these antibodies could play in monitoring disease progression. However, this contrasts with the findings from Rahman and Isenberg[25] which suggested that not all patients with heightened SLEDAI scores demonstrated increased levels of anti-dsDNA antibodies, thus emphasizing the potential complex interplay of other factors in determining disease activity.

Moreover, the relationship between low complement C3 levels and the presence of different autoantibodies warrants attention. Specifically, the high prevalence of dsDNA antibodies in individuals with lower levels of complement C3 suggests a prominent role in the pathophysiology of SLE, a notion supported by Esdaile *et al*.[26] who recognized this antibody as a crucial player in disease progression, particularly noting its potential as a diagnostic marker in clinical practice.

In summation, the intricate relationships between various autoantibodies, complement levels and SLEDAI scores paint a multifaceted picture of the SLE disease landscape. Further research into these relationships might foster enhanced therapeutic strategies and improved monitoring approaches, fostering a more personalized approach to SLE management. This detailed exploration not only corroborates many findings from previous research but also highlights potential avenues for further exploration, particularly focusing on the integration of these markers in clinical practice to enhance the management and prognostication of SLE.

CONCLUSION

The current study elucidates critical associations between disease activity scores, hypocomplementemia and the presence of various autoantibodies in patients with systemic lupus erythematosus (SLE). It is discernible that a considerable fraction of individuals with SLE exhibit moderate to high disease activity, as indicated by the prevalence of SLEDAI scores between 11-20. Moreover, the study substantiates the critical role of hypocomplementemia as a notable marker for evaluating disease activity. Additionally, the presence of specific autoantibodies, particularly anti-dsDNA, demonstrates a strong correlation with heightened disease activity, reinforcing their potential role in the monitoring and management of SLE. Understanding the complex interplay of these parameters could pave the way for nuanced therapeutic strategies and more personalized healthcare interventions for individuals afflicted with SLE. The study had certain limitations. The major limitation was that kidney biopsy was not done to establish the diagnosis of Lupus Nephritis. Also ANCA detection by IIF may have high false positivity due to simultaneous presence of ANA since it can display similar appearance with p-ANCA or a-ANCA. Further studies are required to address this issue and find out more therapeutic option for patients with SLE and ANCA associated vasculitis.

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